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THE JOURNAL OF PEDIATRICS

A MONTHLY JOURNAL DEVOTED TO THE PROBLEMS AND DISEASES OF INFANCY AND CHILDHOOD

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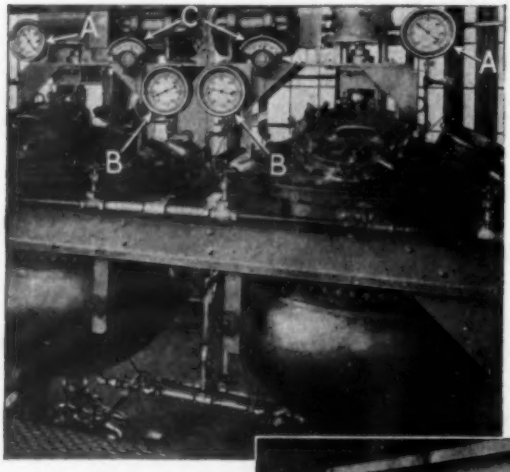
CONTROLLED
Cereal Cookery

If you instruct ten different mothers, "Cook baby's cereal thus and so," there will be ten different results.

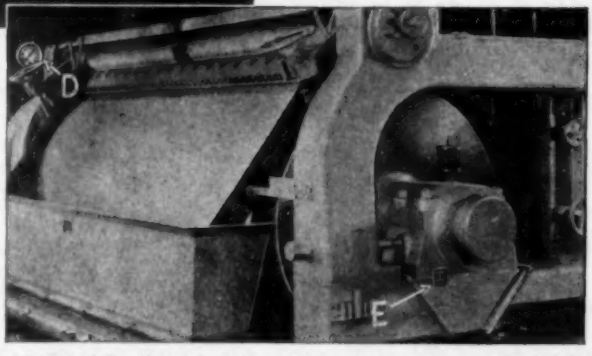
HOME-COOKED cereal is seldom a uniform product . . . because of many uncontrolled factors. The cook, for instance, rarely measures the cereal and the liquid accurately. Nor does she time the cooking carefully. Even if she does, the intensity of the heat varies. Further, the degree of evaporation differs.

Even the type of utensil is a factor. Cooking cereal in a double boiler is likely to cause a surface "skin" to form that is even less digestible than raw starch, Carman *et al* find from digestibility studies *in vitro* of breakfast cereals. They also report that single-boiler cooking for more than 15 minutes actually "decreases digestibility because of the formation of lumps produced by too rapid evaporation of water." This clumping is unavoidable without a condenser and with ordinary household utensils.

Pablum*, in contrast, is manufactured by a patented process and precision methods which insure a thoroughly cooked and uniform cereal. This is substantiated by *in vitro* studies of Ross and Burrill, which show that the starch of Pablum without additional cooking is more rapidly digested than that of oatmeal, farina, cornmeal, or whole wheat cooked 4 hours in a double boiler.



Left—Two double-jacket cookers in which Pablum is steam-cooked under rigid control. Lave steam of uniform pressure and temperature flows into the cookers and displaces air above the cereal thus preventing oxidation and affording protection to vitamins and flavor. A unique paddle-knife constantly agitates the mixture so that a fresh surface is constantly presented to the steam. Note three gauges used in controlling cooking: (A) gauges maintaining uniform steam pressure in tops of cookers; (B) gauges regulating steam pressure in surrounding jackets; (C) thermometers for control of temperature (control of steam pressure and of temperature are both essential.)



Right—One of many drum dryers used in the manufacture of Pablum. After the cereal mixture is steam-cooked it is dropped between revolving steam-heated rollers which roll and dry it in a uniform layer of material. Gauge (D) is used as a check on the steam pressure within the drums. Distance between them is maintained within thousandths of an inch by means of a micrometer plate (E).

*Pablum (Mead's Cereal pre-cooked) is a palatable cereal enriched with vitamin and mineral containing foods, consisting of wheatmeal, oatmeal, wheat embryo, alfalfa leaf, beef bone, brewers' yeast and sodium chloride. Patent pending.

Please send professional card to Mead Johnson & Co., Evansville, Indiana, U.S.A., when requesting samples of Mead products to cooperate in preventing their reaching unauthorized persons.

The Journal of Pediatrics

VOL. 6 APRIL, 1935 NO. 4

Original Communications

STUDIES IN FAT METABOLISM

I. FAT ABSORPTION IN NORMAL INFANTS

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Contents

	PAGE
Introduction	428
Experimental Methods	431
Experimental Observations	432
I. Influence of Size of Fat Particles on Fat Retention	432
II. Effect of Other Food Constituents on Fat Retention	435
A. Minerals	435
B. Protein	438
C. Carbohydrate	441
III. Effect of Variations in Character of Fat Itself	443
A. The Presence of Short Chain (Volatile) Fatty Acids	443
B. Influence of Length of the Carbon Chain	446
C. Relation of Iodine Value and Melting Point to Fat Absorption	446
D. Relative Significance of Total Unsaturation (Iodine Value) and the Percentage of Unsaturated Acids	449
E. The Retention of Certain Odd Carbon Fats	449
F. Observations on Feeding Split Fat	452
G. The Utilization of Ethyl Esters	455
H. A Comparison of Various Natural Fats and Proprietary Fat Mixtures Designed Especially for Infant Feeding	458
IV. Certain Problems Relating to Fat Absorption	464
A. Influence of the Quantity of Ingested Fat—Observations on Fat-Free and High Fat Diets	464
B. The Relation Between the Dried Weight of the Feces, the Fecal Fat, and Fat Absorption	467
C. The Selective Absorption of Individual Fatty Acids	471
D. The Significance of the Fat Partition in the Feces	473
Conclusions	477
References	478

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Introduction

CONFLICTING opinions have been held by pediatricians as to the value of particular fats in infant nutrition. Some have maintained that, aside from their vitamin content, all fats were alike and were valuable only as sources of energy. Others have attributed a physiologic significance to the chemical differences between natural fats; quite popular has been the belief that the fat of human milk represented an ideal, peculiarly suited to the needs of the infant, and no little effort has been expended in devising imitations of this for use in artificial feeding. The evidence in favor of this latter view has been scanty and for the most part unconvincing. Recently, however, there have appeared a number of isolated observations[1] which lend support to the view that fats are not alike physiologically and suggest that some of their components may perform functions hitherto unsuspected. This has made it seem desirable to reinvestigate the question of the comparative value of different fats from as many points of view as possible, and it was with this in mind that the present work was undertaken.

An adequate comparison of different fats should involve not only a study of their ease of assimilation but should also cover their fate after absorption. It is quite possible that fats behave differently in their effect on respiratory metabolism, in ketogenesis, on water metabolism, in immune reactions, and in their hemolytic properties. It is possible that differences exist in the ease with which intolerance can be produced by overfeeding with different fats. Some of these questions we are investigating and will report on subsequently. The present report, however, will deal only with our observations upon absorption from the intestine. Such conclusions as can be drawn from this part of the study in regard to the value of different fats are only tentative and may be considerably modified by further work upon other aspects of fat metabolism.

The literature on comparative fat assimilation is very extensive; observations have been made on children, adults, and experimental animals; and conclusions have been drawn from clinical data, from alimentary lipemic curves, and from balance experiments in which retention has been accurately measured.

Numerous clinical observations have shown that infants will thrive upon a great many different fats, provided that their vitamin requirements are not neglected. Aside from the animal milk fats, animal body fats have been used: suet, lard, tallow, chicken fat, goose fat, egg yolk, and fish oils, notably cod liver oil. Among the vegetable oils, olive oil has been the most extensively used, but there are also reports in which corn oil, cotton seed oil, peanut oil, soy bean oil, sesame oil, cocoanut oil, cocoa butter, and palm oil have been fed, as well as

various mixtures of animal and vegetable fats. No convincing evidence has as yet been adduced that one fat is better handled than another. Only in rare instances was the same infant studied on diets in which the only variable was the fat. Most of the observations were uncontrolled and were continued for relatively short periods. Moreover, in interpreting such clinical reports, it is difficult to eliminate the bias of the observer and the particular care which the subject of an enthusiastically conducted feeding experiment is likely to receive. Such conclusions as have been drawn must be classed as impressions; but, among the conflicting impressions recorded, it is worthy of comment that more than one observer[2] has reached the conviction that olive oil is superior to butter fat at least as far as gain in weight* is concerned.

The data from alimentary lipemic curves are scarcely more conclusive. Lipemia has been followed by chemical methods and by the somewhat less accurate procedure of counting the number of fat particles in an ultramicroscopic field. Only a few observations are recorded in which different fats were studied with an identical technic. Rony and Mortimer[3a] reported that oral administration of egg yolk to dogs caused a more prompt rise in the blood lipids than did olive oil. The comparisons were apparently not made in the same individual subjects. McArthur,[3b] in a small series of adults, using the ultramicroscopic technic, noted that lipemia developed most rapidly after ingestion of cod liver oil, somewhat less rapidly after butter, and least rapidly after goat's milk fat. Schroeder and Evelyn Holt[4] using the ultramicroscopic method made numerous observations on infants. Unfortunately, in many of their experiments the quantity as well as the nature of the fat was varied, a fact which lessens the significance of some of their results. They did find very definitely that a commercial preparation of oleomargarine gave a negligible postabsorptive lipemia as compared with butter or breast milk fat, a fact which they attributed to poor absorption of the oleomargarine. Little reliance can be placed upon the alimentary lipemic curve as an index of fat absorption. The level of the blood fat is determined by the rate of removal of fat from the blood as well as the rate at which it is introduced. The alimentary lipemic curve is notoriously capricious, and it is by no means uncommon to find, both in young children[5] and in adults,[6, 7] individuals who show no postprandial rise, even under circumstances which make

*How erroneous a conclusion can be drawn when gain in weight is used as the sole criterion of absorption is well illustrated by some comparisons we made upon three infants fed first on butter fat and then on the ethyl esters of butter fat. When the ethyl esters were substituted for the triglycerides for a period of twelve days, all three children gained weight more rapidly and continued to exhibit every sign of health. Nevertheless, the retention of fat (figured as percentage of intake) was only 39.3 per cent, 48.3 per cent, and 44.7 per cent, respectively, on the ethyl ester periods as compared with 91.3 per cent, 91.7 per cent, and 84.8 per cent on the butter fat periods. The greater gain in weight may have been a temporary effect due to water retention, which is known to occur when the proportion of carbohydrate to fat absorbed increases. Without the metabolism data one might well have concluded that the ethyl esters were superior to the triglycerides.

it reasonably clear that fat is being absorbed. This phenomenon is more likely to be met with when the quantity of fat given as the test meal is comparable to that of the usual diet and would seem to be due to removal of fat from the blood as rapidly as it is introduced. It is, therefore, possible that a pronounced alimentary lipemia, such as was noted by McArthur after the administration of cod liver oil, may find its explanation in a difficulty of removal of fat from the blood rather than in a more prompt entrance. And, conversely, the failure of alimentary lipemia, noted by Schroeder and Holt[4] after the administration of oleomargarine, may have been due to the ease with which absorbed fat was removed from the blood rather than to diminished absorption.*

To date the only reliable information in regard to the absorption of different fats has been obtained from balance experiments. Experiments on adults and on experimental animals have yielded certain

TABLE I

FAT RETENTION ON COW'S MILK AND BREAST MILK

(FROM DATA OF HOLT, COURTNEY AND FALES)

	PERCENTAGE OF FAT INTAKE RETAINED	PER CENT DISTRIBUTION OF FECAL FAT		
		NEUTRAL FAT	FATTY ACID	SOAP
Average of 8 infants on breast milk	95.8	19.7	27.7	52.6
Average of 28 infants on cow's milk*	90.7	9.6	14.4	76.0

*The figures given here for infants fed on cow's milk differ slightly from those given by the authors in their summary, Reference 12, Tables IX and XVIII. The reason for this is that we have excluded from the series certain infants who received supplements of olive oil.

more or less definite facts, such as a relation between melting point, the degree of unsaturation, the length of the carbon chain, and fat absorption. These will be more fully discussed later in this paper.

The pediatric literature of the last fifty years contains numerous studies on fat metabolism but almost none in which different fats were compared under identical conditions. Holt, Courtney, and Fales[8] compared nut butter and corn oil with butter fat in older children, finding no striking differences. With the exception of Frontali,[9] who substituted olive oil for butter in the Czerny-Kleinschmidt butter-flour mixture and found fat retention somewhat improved, we have been able to find no comparisons of this kind in infants. Many studies have been made on fat retention on cow's milk as compared with breast milk, which studies have in the main confirmed the original findings of Uffelmann.[10] The difference is clearly illustrated by the data of

*Our own metabolism experiments lead us to believe that the latter interpretation is probably the correct one. Although we have not been able to ascertain just what brand of oleomargarine was used by Schroeder and Holt, it has been our experience with preparations on the American market that these are absorbed practically as well as butter fat. This was also the experience of Holt, Courtney, and Fales.[8]

Holt, Courtney, and Fales[11, 12] summarized in Table I. Fat retention is noticeably higher on breast milk, and there are differences in the partition of the fecal fat—the stools on cow's milk containing a higher proportion of soap and less neutral fat and free fatty acid.

The difference in fat retention on cow's milk and on breast milk is not great, but considerable significance has been attached to them. Scarcely an authoritative work in pediatrics is to be found which does not comment upon the relatively difficult digestibility of cow's milk fat, and this doctrine has been responsible for the general abandonment of the cream and top-milk mixtures that were so popular a generation ago. Today the usual practice in artificial feeding is to give not more than 35 per cent of the calories in the form of fat, in contrast to breast feeding in which the infant receives approximately 50 per cent of his calories as fat. A surprising amount of work has been done in devising feedings to obviate one or another of the differences between cow's milk fat and breast milk fat or the factors supposed to affect fat absorption—all without any clear and definite knowledge as to which of these factors was responsible for the difference in retention. Among the procedures used to imitate breast milk may be mentioned: (1) the substitution of various animal and vegetable fat mixtures for butter, in order to emulate the physical and chemical constants of breast milk fat; (2) heating butter to drive off the volatile fatty acids; (3) homogenization of milk to decrease the size of the emulsified fat particles; and (4) demineralization of the milk to diminish the loss of fat as soap in the stools. Most of these procedures are rational and have some experimental basis of fact, but the data in regard to their significance are so conflicting, and so little attempt has been made to study the factors individually, that we undertook to conduct a series of experiments in children in which only one factor at a time was varied.

Experimental Methods

Preparation of Feedings.—In all of our studies designed to compare different fats, a standard basal feeding made from fat-free milk powder, water, and cane sugar* was used. The fat, constituting about 4 per cent of the final diet by weight, was incorporated in the reconstituted skim milk by homogenization,† a standard homogenizer of the Gaulin type being used at 4,000 pounds pressure. The feeding was then autoclaved at about 15 to 20 pounds pressure for half an hour.

Technic of Metabolism Experiments.—These were carried out upon normal male infants between six weeks and eight months of age, who

*The added cane sugar constituted about 8 per cent of the final feeding with the exception of subjects K—n, G—n, and H—t, whose feedings were prepared with the addition of only 5 per cent of cane sugar.

†We wish to take this opportunity of thanking Dr. J. H. Shrader, of the National Dairy Products Research Laboratories, for permission to use their homogenizing apparatus, and also Dr. R. Whitaker, of the same laboratory, for assistance in homogenizing the mixtures.

were placed upon frames designed to permit the separate collection of urine and feces. The metabolism periods were in most instances six days in length and were preceded by a foreperiod of one to four days on the identical diet. In our earlier experiments the stools were marked at the beginning and end of the period by means of charcoal or a dye, such as carmine or vital red, but we subsequently abandoned this procedure when the experimental period was six days or longer, as it seemed to add little to the accuracy of the experiment and the presence of the dye was found to be an inconvenience in the titration of fatty acids.

Analytical Methods.—The determination of total lipids in the food and feces, and of fat partition in the latter, was carried out by a modification of the procedure of Holt, Courtney, and Fales[13] which some of us have described elsewhere.[14]

Iodine Value.—The method of Wijs[15] was used for determinations on fats and fatty acids. Determinations made on unsaponifiable material were done by the pyridine bromide method.[16]

Thiocyanogen Value.—The method of Kaufmann[15] was used. It was found that the determinations of iodine value and thiocyanogen value were unreliable when more than a trace of unsaponifiable matter was present. On this account the determinations of constants on the fecal fat were made upon the fatty acids rather than the total lipids of the feces. In the calculations of the per cent of linoleic, oleic, and saturated fatty acids, the following formulas given by Jamieson[15] were used:

$$\text{Per cent linoleic acid} = 1.104\ (I_2\ \text{No.} - \text{SCN No.})$$
$$\text{Per cent oleic acid} = 1.112\ (2\ \text{SCN No.} - I_2\ \text{No.})$$
$$\text{Per cent saturated acids} = 100 - (\%\ \text{linoleic} + \%\ \text{oleic acids})$$

Experimental Observations

I. The Influence of the Size of Fat Particles on Fat Retention

We have already mentioned the prevailing view among pediatrists that fine subdivision of the fat particles favors fat assimilation, but it may be of interest to examine the sources of this idea. In the first place, emulsification is known to occur normally during digestion of fat, and it is logical to suppose that any assistance in this direction will lighten the work of the body and thus be beneficial. In the second place, the superiority of breast milk to cow's milk in infant feeding has often been attributed to a finer fat emulsion. Most English and American textbooks[17] on pediatrics and infant nutrition carry statements to this effect, of which the following two, taken from recent publications, may be quoted. According to Garrod, Batten, Thursfield, and Paterson,[17f] "much of the indigestibility of cow's milk is due to the fat, the globules being 10 to 15 times as large as those of breast milk." McLean and Fales[17d] in discussing breast feeding and

artificial feeding state that "the fat globules of breast milk are small, therefore easily attacked by the digestive juices." Similar statements are to be found in the continental literature although the testimony on this point is not entirely unanimous.[18] Lastly there are clinical reports[19] in which improvement has followed the use of homogenized milk, the fat particles of which are far smaller than those of any natural milk.

None of this evidence will bear critical analysis. Though it is granted that emulsification occurs normally in the process of fat digestion, there is nothing to indicate that the infant finds difficulty in performing this function himself. Unemulsified fat rarely appears in the feces, and when it does so, this can usually be attributed to some gross defect, such as absence of the external secretion of the pancreas. A fine emulsion is not a prerequisite for fat splitting, for, as Rona and Kleinmann[20] have shown, the rate of lipolysis is independent of the size of the fat particles.

As regards the relative size of the fat globules in breast milk and cow's milk, we recently examined several specimens of each under the microscope and were astonished to find that we could not distinguish between them. We then turned to the literature to find the original data upon which the commonly accepted statement is based. It appears that only a few accurate comparisons of the two milks have been made from this point of view. Rough estimates of particle size date back to the pioneer observations of Donné[21] in 1837, but accurate measurements with counts of the numbers of particles of various sizes have been made only since 1895 when Gutzeit[22] introduced an accurate counting apparatus. Although many of the earlier workers had reported gross differences in particle size, some finding those of human milk to be far smaller and others far greater than those of cow's milk, since the introduction of the refined measurements such differences as have been found have been very small indeed;[23] the variations between different breeds of cows and between individuals are greater than the species variations. Both milks contain particles from 0.3 μ up to 10 μ, with occasional particles as large as 20 μ in diameter; the bulk of the fat consists of particles between 2 μ and 5 μ in size. The more recent reports, such as that of Washburn and Jones,[24] indicate that the average and the extreme size of human milk particles is about the same as in Holstein milk, and slightly less than in Jersey milk.* It is thus

*The figures obtained by Washburn and Jones were as follows:

	MINIMUM SIZE (μ)	MAXIMUM SIZE (μ)	AVERAGE SIZE (μ)
Average of 4 human milks	0.37	8.87	2.29
Herd milk (Holstein)	0.36	9.13	2.14
Herd milk (Jersey)	0.55	10.60	3.81

The slightly larger size of the particles in Jersey milk can be attributed to its higher fat content. Samples of milk containing more fat exhibit particles of slightly larger average size. In making comparisons between different species, it is important that the samples studied should contain approximately equal quantities of fat.

apparent that any superiority human milk may possess for infant feeding is not due to the size of the fat emulsion.

Turning now to the evidence obtained from feeding homogenized milk, we find conflicting testimony. Some pediatricians like Variot[19b] and Ladd[19c] are enthusiastic, whereas others[25] are not impressed. Laboratory observations have failed to settle the question. Washburn and Jones[24] conducted a series of feeding experiments on homogenized milk with young pigs, but the results were so confusing that they were finally forced back to the conclusion that homogenized milk was probably superior because of the gross appearance of the curd, which looked as if it would be easier of digestion. A few observations on fat retention in infants fed on homogenized milk have been made. Chevalier[26] reported improved retention in six infants on this feeding. Usuki,[27] on the other hand, in a single experiment found that absorption was somewhat poorer with homogenized milk. Ladd[19c] refers to some experiments carried out by Laws in Bloor's laboratory which confirmed him (Ladd) in his high opinion of homogenized milk. Details of these experiments have apparently not been published, and we have not succeeded in obtaining further information about them.

Since the question of the effect of particle size on fat absorption is apparently not settled, we undertook to study this. In our experiments we attempted to vary the size of the particles as widely as possible; three different feedings were employed: (1) homogenized cow's milk; (2) unhomogenized cow's milk; and, (3) fat-free cow's milk to which the appropriate amount of fat was added in unemulsified form as melted butter, being either fed by spoon or introduced into the baby's mouth with a syringe. The proportion of fat given was approximately the same in all three feedings. Table II shows the results obtained.

It is apparent that minute subdivision exercised no favorable influence on fat absorption. Differences between the homogenized and unhomogenized milk feedings are altogether negligible. Curiously enough the infants receiving unemulsified fat showed a slightly higher retention than did the other two groups. In part this was probably due to the fact that this particular group included no very young infants, whose retention is appreciably poorer. It is also possible that the difference is due in part to experimental error, for the measurement of the fat intake was not quite as accurate in the experiments with unemulsified fat. Certainly emulsification of the fat fed is unnecessary and adds nothing to the digestibility of the fat.*

*In the experiments described above, it should be noted that autoclaved milk was used throughout. Homogenization can, however, be carried out without heating milk to temperatures that wholly or partially denature the proteins; under these conditions the fine subdivision of the fat alters the character of the protein curd and may increase its digestibility, as compared with raw milk receiving no such thermal treatment. Our experiments do not bear upon this point; they were designed to show only the effect of size of fat particles on fat digestion, with the factor of indigestibility of the protein curd ruled out.

II. The Effect of Other Food Constituents Upon Fat Retention

A. *Minerals.*—Although some evidence[28] of an inverse relationship between soapy stools and fat retention had already been obtained, attention was more strongly focused upon the effect of mineral intake by

TABLE II

INFLUENCE OF SIZE OF FAT PARTICLES ON FAT RETENTION

PERIOD	AGE (MO.)	WT. (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE GM./DAY	FECAL FAT				FAT RETENTION	
						PARTITION				
					GM./DAY	% N. F.	% F. F. A.	% SOAP	GM./DAY	% OF INTAKE RETAINED
Homogenized Cow's Milk										
G—n 2	2	3.60	5	20.64	3.58	3.4	20.8	75.8	17.06	82.7
G—n 7	3½	4.25	5	20.30	2.66	3.7	32.8	63.6	17.64	87.0
K—n 2	1	4.65	6	25.56	3.74	7.2	13.9	78.8	21.82	85.4
K—n 8	3	6.65	4	23.89	3.83	15.1	17.6	69.3	20.06	84.0
H—t* 2	2¼	4.80	8	27.85	4.79	6.9	15.1	78.0	23.07	82.8
McK—a 1	7¾	5.35	8	26.25	2.17	13.2	9.8	77.0	24.08	91.7
McK—a 4	9½	6.85	6	32.90	4.18	18.4	16.0	65.6	28.72	87.3
M—r 1	3¾	4.35	8	21.00	1.82	10.6	12.6	76.8	19.18	91.3
M—r 9	6¾	7.05	5	31.60	3.05	8.4	9.9	81.7	28.55	90.3
W—d 1	4½	5.15	5	30.70	4.68	5.3	26.1	68.6	26.02	84.8
W—d 3	5½	6.00	8	31.50	3.66	7.4	26.5	66.1	27.84	88.4
F—r 3	2¾	3.55	6	15.75	1.43	18.9	14.6	66.5	14.32	90.9
F—r 7	4	4.35	6	20.50	2.14	9.1	11.6	79.3	18.36	89.6
K. J—n 5	4	5.40	6	26.30	1.77	10.6	15.8	73.6	24.53	93.3
J. S—h 13	9	8.16	6	37.01	3.85	9.9	14.7	75.4	33.16	89.6
W. S—h 14	9	7.93	6	32.96	2.92	8.4	14.5	77.1	30.05	91.1
H—k 3	5½	4.70	6	24.91	3.34	7.3	18.4	74.3	21.57	86.6
F—r 1	3	4.93	6	25.14	2.87	13.4	16.7	69.9	22.27	88.5
W—r† 1	5¾	4.80	6	25.13	2.55	7.9	22.8	69.3	22.58	89.8
B—s 1	2½	5.22	5	23.25	2.46	11.6	26.4	62.0	20.79	89.4
C—t 2	4	5.38	6	35.10	4.61	6.8	43.0	50.2	30.49	86.9
Average	*4½*	*5.39*	*6*	*26.58*	*3.15*	*9.7*	*18.6*	*71.4*	*23.44*	*88.2*
Unhomogenized Cow's Milk										
G—n 1	2	3.43	5	20.62	3.00	5.5	29.4	65.1	17.62	85.5
G—n 13	6	4.40	4	23.85	3.26	4.5	12.7	82.8	20.59	86.4
K—n 1	¾	4.33	5	25.18	4.43	4.7	18.5	76.8	20.75	82.4
K—n 14	6½	7.15	4	26.13	4.41	5.4	10.2	84.4	21.72	83.1
H—t 1	2	4.40	10	28.00	2.85	8.2	16.5	75.3	25.15	89.8
H—t 11	6¾	6.90	5	28.29	2.36	8.9	10.8	80.3	25.92	91.6
Average	*4*	*5.10*	*5½*	*25.35*	*3.39*	*6.2*	*16.4*	*77.4*	*21.96*	*86.5*
Unemulsified Butter Given by Spoon or Syringe										
G—n 12A	5¾	4.38	4	24.90	1.93	4.9	21.3	73.7	22.97	92.3
G—n 12B	5¾	4.40	4	24.90	1.92	7.6	14.3	78.1	22.98	92.3
K—n 13A	6	7.05	4	25.00	2.49	6.2	16.0	77.7	22.51	90.0
K—n 13B	6	7.14	4	25.00	2.10	9.9	11.8	77.9	22.90	91.6
H—t 10A	6½	6.80	4	25.16	1.08	7.7	17.1	75.2	24.08	95.7
H—t 10B	6½	6.84	4	25.16	2.23	10.4	11.5	78.1	22.93	91.2
F—r 12	5½	5.07	6	21.60	1.06	24.9	36.8	38.3	20.54	95.1
K. J—n 10	5¾	6.67	6	27.60	1.85	20.0	8.0	72.0	25.75	93.3
Average	*6*	*6.04*	*4½*	*24.92*	*1.83*	*11.5*	*17.1*	*71.4*	*23.08*	*92.7*

*Discharge from ear; infant gained well.

†Slight nasal discharge for two days.

the observations of Bowditch, Bosworth, and Giblin[29] in 1918. These authors concluded that even cow's milk provided an undesirably high mineral intake, its high calcium content causing considerable loss of fat in the feces as insoluble calcium soaps. Bosworth[29] suggested a decalcified milk to avoid this difficulty. Holt, Courtney, and Fales[30] in a preliminary report failed to confirm the striking observations of Bowditch and his collaborators. Their own data showed no great loss of soap on high calcium diets, and they concluded that "serious" loss of fat in the stools on cow's milk does not seem to occur. In a later publication[31] they presented extensive data on calcium and fat retention but did not analyze them from this point of view, being then concerned with the effect of fat upon calcium utilization and excretion rather than with the effect of calcium upon fat metabolism. They did report[32] observations on two children to whom a chalk mixture (calcium carbonate) was given as a supplement; in one subject the fat retention was improved; in the other the reverse was the case. Frontali[33] carried out a few experiments with mineral supplements. To one child he gave as much as 5 gm. of calcium lactate a day without noticeable impairment of fat retention. It thus appears that the evidence in regard to the effect of minerals on fat retention is conflicting.

Our own experiments were planned to answer the question: How much of the difference in fat retention on breast milk and cow's milk is due to the mineral intake? Studies were made in which this was the only variable. In the first series of experiments butter fat was used and three levels of mineral intake were compared: (1) a low ash diet, made by incorporating butter in skimmed breast milk; (2) a medium ash diet, made by incorporating butter in skimmed cow's milk, and (3) a high ash diet in which the butter was incorporated in a skimmed cow's milk base, to which a salt mixture* had been added, approximately doubling the content of each mineral constituent.

A second set of experiments was carried out with breast milk fat which was incorporated: (1) in skimmed breast milk, giving a low mineral intake, and (2) in skimmed cow's milk, giving a medium mineral intake. The results of both series are shown in Table III.

The data show very clearly the inverse relationship between mineral intake and fat retention. A part of the known difference between fat retention on whole cow's milk and whole breast milk can be attributed to the difference in mineral content, but this will not

*The high mineral intake was accomplished by the addition of (a) a solution of potassium and sodium phosphates and (b) a solution of calcium chloride and primary calcium phosphate. The final mineral composition of the feeding as contrasted with the normal control milk formula was as follows:

	Na MG./L	K MG./L	Ca MG./L	Cl MG./L	P MG./L
Standard milk formula	13.6	34.2	27.8	25.8	20.0
High mineral formula	26.3	66.4	52.9	56.9	40.0

TABLE III

INFLUENCE OF MINERALS ON FAT RETENTION

	PERIOD		AGE (MO.)	WT. (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE (GM. PER DAY)	FECAL FAT				FAT RETENTION	
							(GM. PER DAY)	PARTITION			(GM. PER DAY)	PER CENT OF INTAKE RETAINED
								PER CENT N. F.	PER CENT F. F. A.	PER CENT SOAP		
Experiments on Cow's Milk Fat												
Low Ash Diet	G—n	8	3¾	4.23	6	25.70	1.27	9.0	60.8	30.3	24.43	95.1
	K—n	9	3¼	6.64	7	29.41	1.65	13.5	35.2	51.4	27.76	94.4
	Average		*3½*	*5.44*	*6½*	*27.56*	*1.46*	*11.3*	*48.0*	*40.8*	*26.10*	*94.8*
Medium Ash Diet	*Average of 35 exps. in Table II*		*4¾*	*5.49*	*5½*	*25.99*	*2.88*	*9.5*	*18.1*	*72.4*	*23.10*	*88.9*
High Ash Diet	G—n	14	6¼	4.52	6	23.53	5.00	4.8	17.1	78.1	18.53	78.8
	K—n	15	5½	7.40	7	25.76	5.50	4.6	21.6	73.8	20.26	78.7
	H—t	12	7	7.20	7	29.93	3.73	10.7	36.4	52.9	26.20	87.5
	Average		*6¼*	*6.37*	*6 6/7*	*26.41*	*4.74*	*6.7*	*25.0*	*68.3*	*21.66*	*81.7*
Experiments on Breast Milk Fat												
Low Ash Diet	G—n	9	4	4.15	8	22.53	0.74	18.6	59.4	22.0	21.79	96.7
	K—n	10	3¾	6.65	8	26.69	0.67	16.8	28.1	55.2	26.02	97.5
	Average		*4*	*5.40*	*8*	*24.61*	*0.71*	*17.7*	*43.8*	*38.6*	*23.91*	*97.1*
Medium Ash Diet	G—n	5	3¼	4.02	7	17.21	0.96	10.1	37.3	52.5	16.25	94.4
	G—n	6	3½	4.15	6	18.62	1.70	12.2	46.3	41.5	16.92	90.9
	K—n	5	2	5.90	5	25.55	3.55	13.9	20.5	65.4	22.00	86.1
	K—n	7	2¾	6.45	7	23.17	2.69	14.4	23.2	62.4	20.48	88.4
	S—l*	3	9½	6.60	4	23.80	0.67	22.7	25.8	51.5	23.13	97.2
	J. J—n	3	6½	8.25	6	36.00	1.75	9.3	41.6	49.1	34.25	95.1
	K. J—n	14	6½	7.50	6	29.90	1.62	9.2	42.6	48.2	28.28	94.6
	Average		*5*	*6.12*	*6*	*24.89*	*1.85*	*13.1*	*33.9*	*52.9*	*23.04*	*92.4*

*Slightly rancid fat.

account for the entire difference, part of which is due to the fat itself. When the two fats are compared with an identical mineral intake, breast milk fat gives the better retention.

We have not investigated the influence of the individual mineral constituents. Evidence in the literature points to the alkaline earth minerals which form insoluble soaps.

Inasmuch as no correlation between calcium intake and fat retention had been attempted by Holt, Courtney and Fales, it seemed worthwhile to analyze their data[31] from this point of view. In Table IV will be found their data on fat retention as related to the CaO/Fat ratio of the intake in 109 observations on butter fat in normal subjects;

TABLE IV

RELATION BETWEEN CALCIUM INTAKE AND FAT RETENTION

(FROM DATA OF HOLT, COURTNEY & FALES)

$\frac{CaO}{Fat}$ RATIO INGESTED	NUMBER OF OBSERVATIONS	PERCENTAGE OF FAT INTAKE RETAINED	
		AVERAGE	EXTREMES
Normal Infants			
0.021 – 0.040	3	92.1	90.6 – 93.8
0.041 – 0.060	22	89.7	78.9 – 96.4
0.061 – 0.080	5	83.4	70.7 – 94.2
All Normal Subjects			
Below 0.020	6	95.6	94.0 – 97.2
0.021 – 0.040	56	94.3	86.3 – 97.8
0.041 – 0.060	41	91.4	78.9 – 97.5
0.061 – 0.080	5	83.4	70.7 – 94.2
Above 0.080	1	54.4	

thirty of the subjects were infants, the remainder being young children on a mixed diet. Both for the infants and for the series as a whole, the reciprocal relation is apparent. Loss of fat on the diets relatively high in calcium is, as they state, "not serious," but it is nevertheless definite. The data as shown in Chart 1 reveal a certain scattering of the points which is not surprising when one considers that different subjects were used and that the diets were in no sense uniform. On the same graph we have plotted our own average data, which show excellent agreement with those of Holt, Courtney, and Fales. Their results on butter fat average a little higher than ours, a result which may be attributed to the fact that twenty-three of their subjects received small supplements of fat in the form of corn oil, nut butter, olive oil, or cod liver oil.

B. *Protein.*—The influence of protein upon fat absorption has been little studied. A few observations have been made on infants whose protein intake was increased by the addition of milk curd to the food. Frontali studied two infants whose diet was supplemented with 2.5 per cent of plasmon (a proprietary curd preparation); this resulted

in a slight impairment of fat retention. Holt, Courtney, and Fales[34] stated that some of their lowest retention figures in normal infants were those on patients receiving protein milk, but they did not publish data bearing on this point. Through the courtesy of Miss Fales, their unpublished records were made available to us, among which we have been able to find nine experimental periods on five infants who were fed protein milk. These are presented in Table V.

It is apparent that the average fat retention on protein milk (85.7 per cent) is somewhat below that found by the same authors for in-

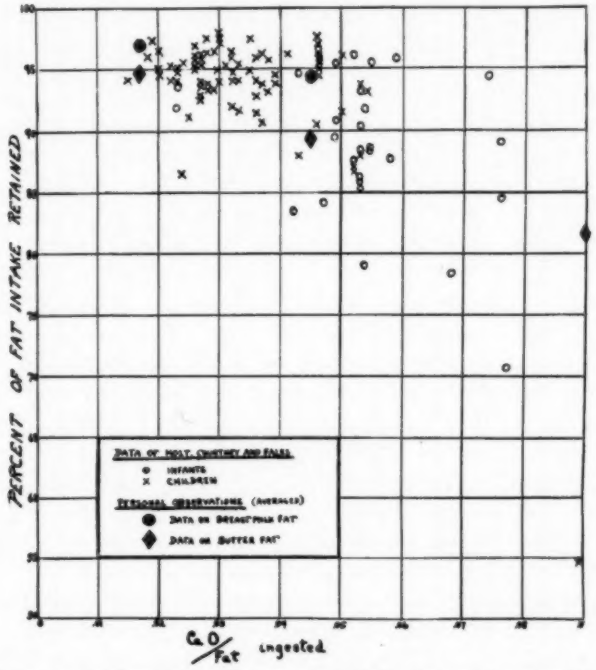

Chart 1.—Relation between CaO: Fat ratio in diet and fat retention.

fants fed on sweet milk mixtures (90.7 per cent). In only one instance was a comparison of protein milk and sweet milk made on the same infant. This patient (A. R.) showed an increase in fat retention when he was returned from protein milk to sweet milk.

Two possible explanations for the lower fat retention on protein milk suggest themselves. It may be that the protein itself stimulates alkaline intestinal secretions,[35] this alkali causing a diversion of fat to the stool in the form of soap. It is also possible that the diminished fat retention is not due to the protein at all, but to the high calcium

TABLE V

FAT RETENTION IN PROTEIN MILK

(FROM UNPUBLISHED DATA OF HOLT, COURTNEY, AND FALES)

CASE	DIAGNOSIS	AGE (MO.)	WEIGHT (GM.)	FEEDING	INTAKE (GM. PER DAY)					% FAT INTAKE RETAINED
					PROTEIN	FAT	SUGAR	FLOUR	CALCIUM	
W. G.–15	Rickets; marasmus	10	3940	Protein milk; cereal	31.7	15.1	15.7	11.4	1.04	87.8
J. L.–22e	Convalescent from vomiting and diarrhea	8	4990	Protein milk; sugar; barley flour (raw)	38.4	29.4	24.5	31.5	1.31	89.6
J. L.–22f	Convalescent from vomiting and diarrhea	8½	4910	Protein milk; sugar; barley flour (raw)	41.5	31.7	26.7	36.0	1.42	85.9
A. A.–22a	Marasmus	6½	3920	Protein milk; barley flour (raw)	43.7	31.8	19.1	18.0	1.54	80.8
A. A.–22b	Marasmus	6¾	4060	Protein milk; barley flour (raw)	43.7	31.3	18.9	25.4	1.52	85.7
A. A.–22c	Marasmus	7	4160	Protein milk; barley flour (raw)	42.2	29.8	17.9	30.0	1.45	85.6
A. R.–19b	Convalescent from marasmus	7¼	5300	Protein milk; barley flour (raw)	47.3	31.9	19.2	25.1	1.55	87.9
A. R.–19c	Convalescent from marasmus	7½	5410	Protein milk; barley flour (raw)	48.0	31.9	19.2	32.2	1.55	85.2
A. R.–19d	Convalescent from marasmus	7¾	5600	Protein milk; barley flour (raw)	44.6	28.9	17.4	38.9	1.40	82.9
									Average	*85.7%*
				Observation on Patient A. R. After Return to Sweet Milk Formula						
A. R.–19e	Convalescent from marasmus	8	5680	Sweet milk; barley flour (raw)	24.9	21.6	14.4	45.0	0.74	90.2%

intake. Approximately twice as much calcium is ingested on a diet of protein milk as upon a formula of diluted cow's milk. The magnitude of the diminution of fat retention in the experiments of Holt, Courtney, and Fales was in keeping with the view that this was due entirely to the higher calcium intake. In order to test this point further we studied several infants on diets in which the mineral factor could be excluded, diets in which isoelectric protein—casein or gelatin —was added. The results are given in Table VI.

Inspection of the data reveals no consistent change brought about by the addition of isoelectric protein. The retention of fat is sometimes a little better, sometimes a little worse, and at other times identical with that on the control period. One appears justified in attributing the effect of protein milk entirely to its calcium content rather than to any influence of the protein itself. This conclusion is supported by the studies Courtney and Moore[36] made upon three infants who were given a synthetic food in which a high protein intake was accomplished by the addition of sodium caseinate. Although the protein content of this food was well in excess of that of protein milk, the diet failed to cause any appreciable falling off of fat retention until the patients developed fever.

C. *Carbohydrate.*—The claim has been made that starch when given in large quantities exerts an unfavorable influence on fat absorption. Stolte[37] studied three infants fed on the Czerny-Kleinschmidt butter-flour mixture and found low retentions of fat (70 per cent to 83 per cent of the intake). Noack[38] obtained similar low figures with this food, but there is reason to believe that his subjects were abnormal, for he obtained even lower retentions on standard cow's milk formulas. Frontali[39] made observations on four infants fed on the butter-flour mixture who retained 92.6 per cent, 88.3 per cent, 78.8 per cent, and 82.2 per cent of their fat intake, respectively (average 85.5 per cent). It seems possible that when starch is used as an emulsifying agent for the fat, as is the case with butter-flour feedings, a certain amount of fat may be carried out with undigested starch. On the other hand, when starch is added to milk and not used to emulsify the fat (Freund[40]), such loss of fat seems to be negligible. Among unpublished data of Holt, Courtney, and Fales, we have found records of observations on four infants who were fed sweet cow's milk with additions of barley flour (from 27 to 45 gm. a day). In these experiments the fat retention was 85.2, 90.2, 90.3, and 87.7 per cent (average 88.4 per cent), figures comparable to those obtained with sweet cow's milk and added sugar.

A few observations have been made on the influence of other polysaccharides and sugars upon fat retention. Usuki[41] studied a number of carbohydrate mixtures, but the differences he obtained were not

TABLE VI

INFLUENCE OF PROTEIN ON FAT RETENTION

DIET	PERIOD	AGE (MO.)	WT. (KG.)	LENGTH OF PERIOD (DAYS)	INTAKE (GM. PER DAY)		FECAL FAT				FAT RETENTION	
					PROTEIN	FAT	GM./DAY	% N. F.	% F. F. A.	% SOAP	GM./DAY	% OF INTAKE RETAINED
A. Control Periods												
Milk and cane sugar formula	J. S—h 13	9	8.16	6	30.3	37.01	3.85	9.4	14.7	75.4	33.16	89.6
	F—r 1	3	4.93	6	22.0	25.14	2.87	13.4	16.7	69.9	22.27	88.5
	W—r 1	5½	4.80	6	22.0	25.13	2.56	7.9	22.8	69.3	22.58	89.8
	R. S—h 1*	1½	4.05	5	17.4	19.37	3.29	7.2	20.5	72.3	16.08	83.0
	C—t 2	4	5.38	6	28.7	35.10	4.61	6.8	43.0	50.2	30.49	86.9
	W. S—h 14	9	7.93	6	27.0	32.96	2.92	8.4	14.5	77.1	30.05	91.1
	Average	*5½*	*5.88*	*5.8*	*24.6*	*29.12*	*3.35*	*8.9*	*22.0*	*69.0*	*25.77*	*88.2*
B. Periods With Added Protein												
Milk and sugar formula plus isoelectric casein	J. S—h 14	9½	8.40	6	58.6	34.44	3.59	7.8	21.8	70.4	30.85	89.5
	F—r 4	4	5.93	6	50.3	28.80	2.04	6.9	20.6	72.5	26.76	92.9
	W—r 4	7	5.80	6	50.2	28.73	2.48	4.0	35.0	61.0	26.25	91.4
	R. S—h 4	2½	4.89	6	41.9	24.00	2.58	9.8	24.8	65.4	21.42	89.2
	C—t 3	4½	5.68	6	54.5	31.98	6.96	9.2	29.5	61.3	25.02	78.3
Plus isoelectric gelatin	W. S—h 15	9½	8.11	6	54.5	34.32	4.20	7.7	27.0	65.3	30.12	87.7
	Average	*6½*	*6.47*	*6*	*51.7*	*30.38*	*3.64*	*7.6*	*26.4*	*66.0*	*26.74*	*88.2*

*Period terminated one day early because a parenteral infection developed.

very striking, his most convincing finding being a somewhat impaired fat retention on a feeding which contained malt soup extract. Frontali[33] in one subject found that glucose exercised an unfavorable influence as compared with lactose and maltose. We ourselves have carried out a few experiments designed to compare the effect of cane sugar, lactose, and a malt-dextrin preparation (dextri-maltose) on fat retention. The results are given in Table VII.

TABLE VII

INFLUENCE OF VARIOUS SUGARS ON FAT RETENTION

PERIOD		AGE (MO.)	WT. (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE (GM./DAY)	FECAL FAT				FAT RETENTION	
							PARTITION				
						(GM./DAY)	% N. F.	% F. F. A.	% SOAP	GM./DAY	% OF INTAKE RETAINED
A. Cane Sugar											
W—r	1	5¾	4.80	6	25.13	2.56	7.9	22.8	69.3	22.58	89.8
F—r	1	3	4.93	6	25.14	2.87	13.4	16.7	69.9	22.27	88.5
R. S—h	1*	1¾	4.05	5	19.37	3.29	7.2	20.5	72.3	16.08	83.0
Average		*3½*	*4.59*	*5⅞*	*23.21*	*2.91*	*9.5*	*20.0*	*70.5*	*20.31*	*87.1*
B. Dextrimaltose											
W—r	2	6	5.09	6	24.00	2.40	11.1	20.3	68.6	21.60	90.0
F—r	2	3¼	5.25	6	24.00	2.33	12.5	20.4	67.1	21.67	90.4
R. S—h†	2	2	4.38	6	19.20	2.43	7.7	17.1	75.2	16.77	87.3
Average		*3¾*	*4.91*	*6*	*22.40*	*2.39*	*10.4*	*19.3*	*70.3*	*20.01*	*89.2*
C. Lactose											
W—r	3	6¼	5.16	6	25.20	2.45	10.7	30.5	58.8	22.75	90.3
F—r	3	3½	5.55	6	25.20	2.87	11.2	35.5	53.3	22.33	88.6
R. S—h	3	2¼	4.60	6	21.60	3.16	8.1	30.2	61.7	18.44	85.4
Average		*4*	*5.10*	*6*	*24.00*	*2.83*	*10.0*	*32.1*	*57.9*	*21.17*	*88.1*

*Period terminated one day early because of development of parenteral infection.
†No evidence of respiratory infection persists.

No significant difference in fat retention on these different diets is noticeable with the exception of patient R. S—h, who did not retain fat as well on cane sugar as on the other two sugars. This may have been due to the fact that he was affected to a slight extent by the mild parenteral infection which made its appearance at the end of the period. In all three babies the stools contained slightly more free fatty acid in the lactose periods. This is probably due to an increase in volatile fatty acid derived from carbohydrate fermentation, a subject which has recently been studied by Gerstley.[42]

III. THE EFFECT OF VARIATIONS IN THE CHARACTER OF THE FAT ITSELF

A. *The Presence of Short Chain (Volatile) Fatty Acids.*—Free fatty acids of 10 carbon atoms or less are volatile with steam. The measure of their presence in a mixed fat is the Reichert-Meissl number. In

natural fats this differs widely; for instance, butter contains far more of the short chain acids (R.M. about 30) than does breast milk fat (R.M. less than 2).

Free volatile fatty acids are found in infant's stools; they are slightly more abundant in those of infants fed on cow's milk; in diarrheal states, however, their quantity is greatly increased. Certainly the greater part of the volatile acids of the stool arises from fermentation of carbohydrate; according to one view,[43] which has yet to be disproved, they are the irritants which cause peristalsis. But the possibility that some at least of the volatile acids of the stool might arise from their ingestion as such has led to more than one attempt to eliminate fats containing them from the infant's diet. Gerstenberger and Ruh[44] devised a fat mixture for artificial feeding, in which among other things the Reichert-Meissl number did not exceed that of breast milk. In the preparation of the Czerny-Kleinschmidt butter-flour mixture[45] the butter is heated until bubbling ceases, the bubbling being presumably caused by the expulsion of volatile fatty acids.*

Our interest lay in determining to what extent, if any, a fat showing a high Reichert-Meissl number is harmful when fed. We attempted to accentuate such effects as these substances might produce by increasing their quantity to approximately twice that of ordinary butter. This was done in two ways: (1) by adding tributyrin to butter and (2) by adding a distillate of *free* volatile acids obtained from another lot of butter. On neither feeding were clinical disturbances noted, the children remaining quite normal. The tributyrin imparted a bitter taste to the milk so that it was necessary to accustom the babies to it gradually, but once this was done it was well taken. The test given was probably a more exacting one than would have been the case had we been able to increase the volatile acids in the identical form in which they occur in butter. Presumably free fatty acids would be more irritating than when combined, and a triglyceride composed entirely of short chain acids (tributyrin) might well be more irritating than triglycerides such as exist in butter where long and short chains occur in the same molecule.

The results indicate that volatile fatty acids, even in quantities well above those present in butter, are not to be feared. Table VIII shows that fat retention in these experiments remained within the normal limits, indicating that the volatile acids are well absorbed. This is further attested to by the low Reichert-Meissl number of the stool fat in the tributyrin periods, as contrasted with the fat of the diet. The

*Personal observations indicate that the bubbling which occurs when butter is so heated is due to the escape of steam rather than of volatile fatty acids. The heating procedure recommended is quite ineffectual in reducing the Reichert-Meissl number of butter; a lot so heated had an R.M. number of 31 after heating as compared with 33 before heating. This result is not surprising when one stops to consider that the volatile acids in butter are not free, but combined as triglycerides, which have high boiling points.

TABLE VIII

INFLUENCE OF VOLATILE FATTY ACIDS ON FAT RETENTION

FEEDING	PERIOD	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	INGESTED FAT		FECAL FAT					FAT RETENTION	
					QUANTITY GM./DAY	REICHERT-MEISSL NUMBER	QUANTITY GM./DAY	PARTITION % N. F.	PARTITION % F.F.A.	PARTITION % SOAP	REICHERT-MEISSL NUMBER	GM./DAY	% OF INTAKE RETAINED
Free volatile fatty acids added to butter	H—t 6	4½	5.67	5	23.37	53.1	3.52	6.6	14.6	78.9		19.85	84.9
	H—t 7	5	6.09	6	32.60	53.1	3.04	8.8	39.5	51.7		29.56	90.7
Tributyrin added to butter	W—d 4	9½	7.80	6	37.00	58.0	3.67	8.4	20.8	70.8	9.0	33.33	90.1
	K. J—n 11	5½	6.90	6	27.60	58.0	2.70	7.3	12.3	80.4	3.6	24.90	90.2
Control observations on butter alone	Average of 35 experiments	4½	5.49	5½	25.99	31.4	2.89	9.5	18.1	72.4	1.7*	23.10	88.9

*Average of four experiments.

R.M. value of the stool fat in these experiments is not far above that in the control periods and is much less than may occur in cases of diarrhea. These facts are in harmony with the view that the volatile fatty acids of the stool are derived chiefly from the carbohydrate rather than the fat of the diet.

B. *The Influence of Length of the Carbon Chain.*—As far as we are aware, this question has not been studied in man, and only a few observations have been made in animals. Among the saturated straight chain fatty acids it appears that absorption falls off to some extent when the chain becomes as long as 16 carbon atoms (palmitic) and even more so with the 18 carbon (stearic) acid. In dogs Arnschink[46] found that tristearin was only from 9 to 14 per cent absorbed, whereas Lyman[47] observed that in the dog tripalmitin was only slightly less well absorbed than was lard. Levites,[48] using dogs, compared the absorption of free palmitic and stearic acids and their sodium soaps; palmitic acid was absorbed to the extent of 63 to 78 per cent, whereas stearic acid was absorbed only 19 to 35 per cent. The difference was also present when the sodium soaps were compared, though it was less marked. Frank[49] and Müller and Murschhauser,[50] working with dogs, found that ethyl palmitate was better absorbed than ethyl stearate; and in this laboratory, Cox,[51] working with white rats, found that the 12 carbon ethyl laurate was very completely absorbed in contrast to ethyl stearate.

Our studies in children were made on two almost completely saturated fat mixtures: (1) cocoanut oil (iodine number, 8) which contains a considerable proportion of acids with only 12 and 14 carbon atoms and has a mean molecular weight of 218; and (2) a mixture of tripalmitin and tristearin (approximately 2:1) which had an iodine number of 2 and a mean molecular weight of 278. Table IX shows that the material containing the shorter chain fatty acids is more completely absorbed.

C. *Relation of Iodine Value and Melting Point to Fat Absorption.*—A number of observations in the literature indicate that unsaturated fats are more readily absorbed. In 1889 Arnschink[46] had shown that dogs absorb olive oil better than they do tristearin. Munk and Rosenstein[52] in 1891 in a patient with a chyle fistula noted that olive oil was better absorbed than other more saturated fats which they used. Schabad and Soroschowitch[53] in 1911 observed in infants an improved retention of fat when olive oil was added to the food, and, more recently, Frontali[9] found that the substitution of olive oil for butter in the Czerny-Kleinschmidt butter-flour mixture increased fat retention. More impressive evidence upon this point can be obtained from the

TABLE IX

INFLUENCE OF LENGTH OF FATTY ACID CHAIN UPON FAT RETENTION

FAT FED	PERIOD	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	INGESTED FAT		FECAL FAT				FAT RETENTION	
					QUANTITY GM./DAY	MEAN MOLECULAR WEIGHT	GM./DAY	PARTITION			GM./DAY	% OF INTAKE RETAINED
								% N. F.	% F. F. A.	% SOAP		
Cocoanut oil	K—n 3	1½	5.13	10	19.88		3.87	4.3	30.5	65.2	16.01	80.5
	S—l 1	9½	6.42	6	30.80	218	1.75	7.2	36.4	56.4	29.05	94.3
	W—d 5	9¾	8.00	5	33.40		2.88	4.2	30.2	65.6	30.52	91.4
	Average	7	*6.52*	7	*28.03*		*2.83*	*5.2*	*32.4*	*62.4*	*25.19*	*88.7*
Tripalmitin—tristearin	H—t 5	3½	5.55	5	24.25		9.36	6.5	32.7	60.8	14.89	61.4
	J. J—n 2	6½	8.00	3	37.40	278	14.43	17.8	32.0	50.2	22.97	61.5
	K. J—n 13	6½	7.27	6	30.00		11.52	5.5	43.2	51.3	18.48	61.6
	Average	7¼	*6.94*	*5*	*30.55*		*11.77*	*9.9*	*36.0*	*54.1*	*18.78*	*61.5*

data of Langworthy and his associates,[54] who studied a large series of natural fats in adults. In Chart 2 we have plotted their average retention figures for various fats having a mean molecular weight above 270 against the iodine value of the fat.* Similar data of our own in infants are plotted in the same graph. The two sets of data are in good agreement and illustrate the relation between retention and unsaturated linkages in a fat.

It is easy to suppose that greater ease of absorption of short chain fats and unsaturated fats is due to a property they possess in common —a low melting point. Indeed in the past the melting point has been generally regarded as the factor limiting absorption. It was originally maintained[55] that fats melting above the body temperature were not

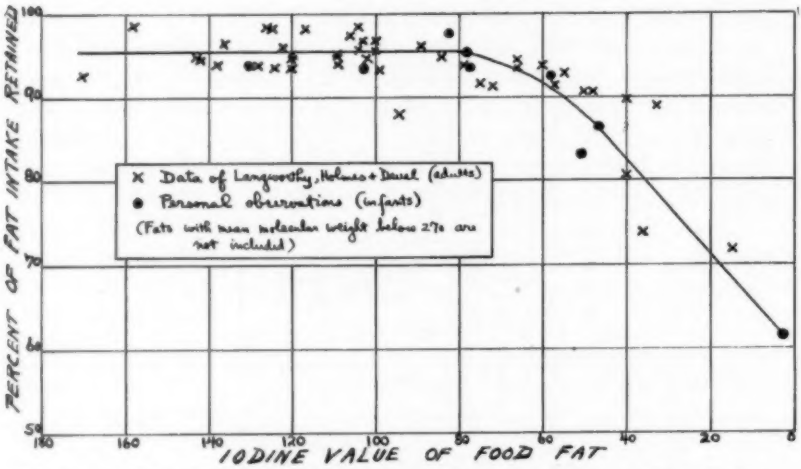

Chart 2.—Relation between iodine value of food fat and fat retention (average figures).

readily absorbed, but this was subsequently found not to be strictly true. Langworthy and his associates[54] in their study of hydrogenated oils noted impaired retention only when the melting point rose above 45° or 50° C. From data hitherto available it has not been possible to decide whether it was the lower melting point or the accompanying difference in chemical constitution which favored absorption, but we now wish to present evidence which indicates that it is the chemical difference rather than the difference in melting point which is significant.

In the course of hydrogenation of highly unsaturated fats, glycerides of elaidic acid are formed which, though isomeric with those of oleic

*Values for constants of the fats they used were not given by Langworthy. We have, therefore, used values taken from the literature and have included only fats for which the constants are reasonably well known.

acid and containing likewise one double bond, nevertheless melt at a comparatively high temperature. By using partially hydrogenated corn oil,* on the one hand, and a 2:1 mixture of tripalmitin and tristearin, on the other, we have been able to compare two fats of practically identical melting point which differed widely in their content of unsaturated fatty acid. The difference in retention is shown in Table X. It is apparent that the presence of double bonds ensures good absorption† regardless of the high melting point.

D. *Relative Signficance of the Total Unsaturation (Iodine Value) and the Percentage of Unsaturated Fatty Acids.*—It seemed of interest to determine whether absorption is determined by the total number of double bonds in the fat (iodine value) or by the percentage of fatty acids which contain one or more double bonds. In order to test this point we compared two fats with an identical iodine value, one consisting almost entirely of a one double bond unsaturated fat (a very pure olein‡) and the other a mixture containing more highly unsaturated fatty acids and saturated fatty acids (made by mixing corn oil and butter). If the determining factor were the percentage of fatty acids containing one or more double bonds, instead of the iodine value, one would expect the pure olein to be better absorbed than the corn oil-butter fat mixture. The data obtained indicate that this is the case (Table XI).

Neglect of this possibility has led at least one set of imitators of breast milk fat into error. Gerstenberger and Ruh,[44] in their preparation known as "S. M. A.," chose to imitate the iodine value of breast milk fat (which is largely due to the one double bond olein) by a mixture containing highly unsaturated fatty acids (from cod liver oil) and saturated fatty acids (obtained from tallow). They apparently overlooked the fact that such a mixture as theirs contains (according to our measurements) between 10 and 15 per cent more of the less readily absorbed saturated fatty acids than does average breast milk fat. We believe that this fact explains in part our findings on the retention of S. M. A. fat, which are presented in another section.

E. *The Retention of Certain Odd Carbon Fats.*—Since our studies on the utilization of certain odd carbon fats by infants and the methods of preparation of these materials are presented in more detail elsewhere,[56]

*This material, known as "Argo," was supplied by the courtesy of the Corn Products Refining Company.

†It may be noted that the retention figures on hydrogenated corn oil (83 per cent) are slightly lower than what we have usually found (from 90 to 92 per cent) on olein-containing fats of similar iodine number, but of far lower melting point. It is possible that the higher mean molecular weight of this preparation will account for this slightly poorer retention.

‡This material consisted largely of triolein, but a considerable amount of monoglyceride and diglyceride was also present.

TABLE X

RELATIVE IMPORTANCE OF IODINE VALUE AND MELTING POINT OF A FAT IN DETERMINING FAT RETENTION

FAT FED				PERIOD	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE GM./DAY	FECAL FAT				FAT RETENTION	
	MELTING POINT	IODINE VALUE	MEAN MOLECULAR WEIGHT						GM./DAY	PARTITION % N. F.	% F. F. A.	% SOAP	GM./DAY	% OF INTAKE RETAINED
Partially hydrogenated corn oil (Argo)	50° C.	50.2	283	J. J—n 1	5¾	7.75	6	37.20	6.90	11.8	22.8	65.4	30.30	81.5
				K. J—n* 12	6	7.10	6	28.60	4.43	11.8	15.9	72.3	24.17	84.5
				Average	*6*	*7.43*	*6*	*32.90*	*5.67*	*11.8*	*19.4*	*68.8*	*27.23*	*83.0*
Tripalmitin—tristearin (2:1)	52° C.	2.4	278	H—t 5	3¼	5.55	5	24.25	9.36	6.5	32.7	60.8	14.89	61.4
				J. J—n 2	6½	8.00	3	37.40	14.43	17.8	32.0	50.2	22.97	61.5
				K. J—n 13	6¼	7.27	6	30.00	11.52	5.5	43.2	51.3	18.48	61.6
				Average	*5¼*	*6.94*	*4⅞*	*30.55*	*11.77*	*9.9*	*36.0*	*54.1*	*18.78*	*61.5*

*This infant had a slight coryza for part of the period, but it did not seem to affect digestion or gain in weight.

TABLE XI

RELATIVE SIGNIFICANCE OF THE TOTAL UNSATURATION (IODINE VALUE) AND THE PERCENTAGE OF UNSATURATED FATTY ACIDS

FAT FED										FECAL FAT					FAT RETENTION		
	IODINE VALUE OF FATTY ACIDS	SCN VALUE OF FATTY ACIDS	PERCENTAGE OF UNSATURATED FATTY ACIDS	PERIOD	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE GM./DAY	GM./DAY	PARTITION % N. F.	% F. F. A.	% SOAP	IODINE VALUE OF FATTY ACIDS	GM./DAY	% OF FAT INTAKE RETAINED	COMMENTS
Corn oil—butter mixture	87.3	52.8	58.4	J. S—h 3	2¾	4.00	6	19.23	4.56	34.0	13.6	52.4	52.7	14.67	76.3	Twin
				W. S—h 3	2¾	3.70	6	18.98	3.46	24.7	20.0	55.3	67.1	15.52	81.8	Twin
				H—r 6	4½	4.75	6	21.80	1.22	21.8	37.3	40.9	42.5	20.58	94.4	Aural discharge. Digestion O. K.
				K. J—n 17	7¼	8.05	3	27.50	3.63	21.8	39.8	38.4	48.5	23.87	86.8	
				Average	*4¼*	*5.13*	*5¼*	*21.88*	*3.22*	*25.6*	*27.7*	*46.7*	*52.7*	*18.66*	*84.8*	
Pure olein	89.9	86.5	96.1	J. S—h 4	3½	4.40	6	24.00	2.66	53.0	27.1	19.9	73.8	21.34	88.9	Twin
				W. S—h 4	3½	4.20	6	23.75	5.04	41.4	46.3	12.3	82.5	18.71	78.8	Twin. Otitis and loose stools developed at end of period.
				H—r 7	5	5.15	5	23.99	0.77	27.8	27.2	45.0	60.0	23.22	96.8	Aural discharge part of the time. Digestion O. K.
				K. J—n 16	7	7.90	3	28.10	0.51	47.2	23.2	29.6	68.5	27.59	98.2	
				Average	*4¾*	*5.41*	*5*	*24.96*	*2.25*	*42.3*	*31.0*	*26.7*	*71.2*	*22.72*	*90.7*	

they will only be summarized here. Briefly, we found that the glyceride of tridecylic acid (C_{13}), in contrast to the findings of Verkade[57] on adults, was toxic although fairly well absorbed (55.5 per cent of the intake). The ethyl ester of margaric acid (C_{17}) was not toxic, but was absorbed to the extent of only 25 to 30 per cent of the intake (Table XII). A 1:4 mixture of the glycerides of pentadecylic and margaric acids (C_{15} and C_{17}) was well tolerated and gave rise to no toxic symptoms when the intake was kept at 4 per cent. When this material was fed in the form of ketogenic diet, the feeding was not well taken, but even so 73.3 per cent of the intake was retained.

On this diet ketone bodies made their appearance just as would have been anticipated with even carbon fats. The possibility could not be excluded that the ketone bodies were formed from the patient's body fat rather than from the ingested fat although the latter seemed the more probable explanation and was in harmony with the observations of Verkade who found evidence for both beta-oxidation and omega-oxidation in the case of his odd carbon fats. From these few experiments one cannot draw accurate deductions as to the relative ease of absorption of odd and even carbon fats. It may be that, other factors being equal, the odd carbon fats are as well absorbed. The somewhat impaired retention noted with the odd carbon glycerides may well have been due to their more or less toxic action. With the ethyl esters of margaric acid we observed poorer retention than with the ethyl esters of butter (see Section H), but this would be expected since the odd carbon material had a higher mean molecular weight and contained no unsaturated linkages.

F. *Observations on Feeding Split Fat.*—Poor fat retention and the presence of much unsplit fat in the feces is found in diarrheal states and in conditions with a deficiency of the external secretion of the pancreas. Lack of pancreatic lipase, in the latter instance, and inadequate time for it to act, in the former case, would explain the poor fat splitting, and it seemed probable that inadequate fat splitting was the cause of the poor absorption. These considerations led us to investigate the practicability of feeding split fat, an undertaking which promised success in view of the encouraging studies of Levites[48] on dogs. Levites found that free palmitic and stearic acid were distinctly better retained than their triglycerides; still better results were obtained with the sodium soaps, results which were quite comparable to those obtained with the readily absorbable fats. Aside from the precaution that the soap-containing diets had to be made palatable, he noted no difficulties and no untoward results.

TABLE XII

OBSERVATIONS ON THE RETENTION OF CERTAIN ODD CARBON FATS

FAT FED	PERIOD	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE GM./DAY	FECAL FAT				FAT RETENTION		ACETONE IN URINE	COMMENTS
						GM./DAY	PARTITION			GM./DAY	% OF INTAKE RETAINED		
							% N. F.	% F. F. A.	% SOAP				
Glyceride of C_{13}	H—r 4	3¾	4.15	4	19.22	8.56	22.8	27.6	49.6	10.66	55.5		Patient did not thrive on this feeding. Stools loose; vomited some. No gain in weight.
Glycerides of C_{15} and C_{17} (1:4)	H—k 7	8	7.00	3	38.30	10.23	28.2	71.8		28.07	73.3	+++	Thrived fairly well. Some refusal of food.*
Ethyl esters of C_{17}	McK—a 7	10	6.80	3	38.00	28.60	35.7	22.7	41.6	9.40	24.8	0	Rapid gain in weight following high ethyl ester period.
	McK—a 8	10	7.20	3	40.00	28.48	14.3	38.3	47.4	11.52	28.8	0	Still gaining weight rapidly.
Ethyl esters of C_{17} fed at high level	McK—a 6	9¾	6.50	3	95.90	71.00	65.5	25.5	9.0	24.90	26.0	+ to ++	Losing weight after start of high fat diet.†

*Ketogenic diet, Woodyatt ratio—2.5.
†Ketogenic diet, Woodyatt ratio—3.2.

In all we performed three experiments with split fat. In the first one, a mixture of palmitic and stearic acids* (approximately 2.1) was substituted for the milk fat. The material was homogenized without difficulty, but upon autoclaving, coagulation of the milk occurred so that sieving was necessary before it could be fed. Within a few hours after the experiment was started, the child developed diarrhea, which by the third day had become so severe that it was necessary to terminate the experiment, whereupon the diarrhea promptly subsided.

The metabolism study, though less accurate than our other studies because of the shortness of the period (forty-eight hours), is rather illuminating. Fat retention, as might have been anticipated in view of the diarrhea, was poor, being only 8.8 per cent. But altogether unexpected was the finding that a large part of the unabsorbed fatty acid appeared in the stool in the form of soap.

We did not feel justified in attempting further studies with free fatty acids in these quantities. Moreover, the above experiment indicated that little was to be expected from feeding palmitate and stearate in the form of soaps. However, inasmuch as Levites had reported better results with sodium oleate than with either free oleic acid or the soaps of palmitic or stearic acid, we undertook to feed two babies sodium oleate in place of the milk fat. The infants made no objection to the taste of these feedings, which were quite unpalatable to adults.† They continued to thrive and gain weight and their stools were only slightly softer than normal. However, they showed signs of thirst and a slight degree of fever (Charts 3 and 4) on an intake of water that had been previously sufficient; when allowed water ad libitum they consumed considerably more than before. Fat retention, as shown by the metabolism study, was fairly complete in both subjects. We have no explanation for the fact that a considerable amount of the stool fat in these periods consisted of neutral fat plus unsaponifiable matter.

On the whole we are not impressed with the feasibility of feeding split fat (Table XIII). The irritant properties of free fatty acids when all the fat is so supplied and the high water requirements when the fat is fed as sodium soap appear to be serious objections, at least as far as their use in diarrhea is concerned.

There is reason to believe, however, that smaller quantities of free fatty acids can be well tolerated—perhaps sufficient for the acidification of milk; it is rather remarkable in view of the great assortment of acids suggested for that purpose that the fatty acids should have

*This material was supplied through the courtesy of the Procter and Gamble Company.

†The aversion to the taste of soap seems to be acquired at a later period of life, for we have often seen young children eat considerable quantities of toilet soap with apparent pleasure.

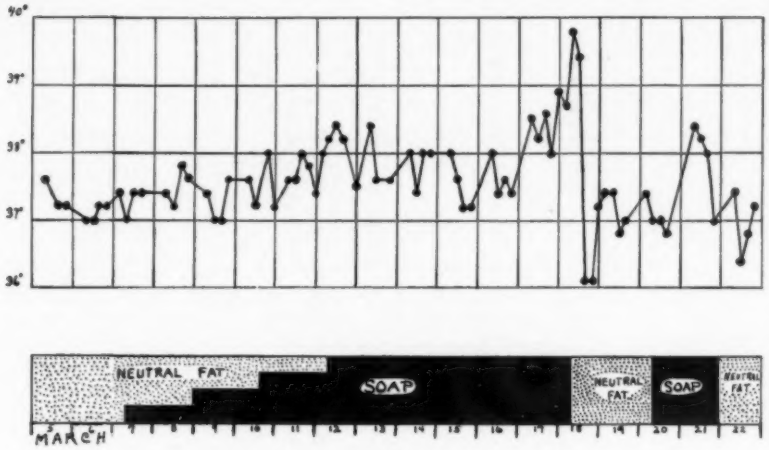

Chart 3.—Twin J. S—h.

been overlooked. Some years ago von Mering[58] recommended the use of a mixture of olive oil plus 6 per cent free oleic acid (lipanin), and subsequent reports[59] in the German pediatric literature indicate that this was well tolerated.

G. *The Utilization of Ethyl Esters.*—As far as we are aware, ethyl esters have been studied only in animals. A number of balance experiments are on record. Frank[49] in 1898 fed ethyl palmitate and ethyl stearate to dogs and observed retentions of 75 per cent and 12 per cent, respectively. He made the interesting observation that when

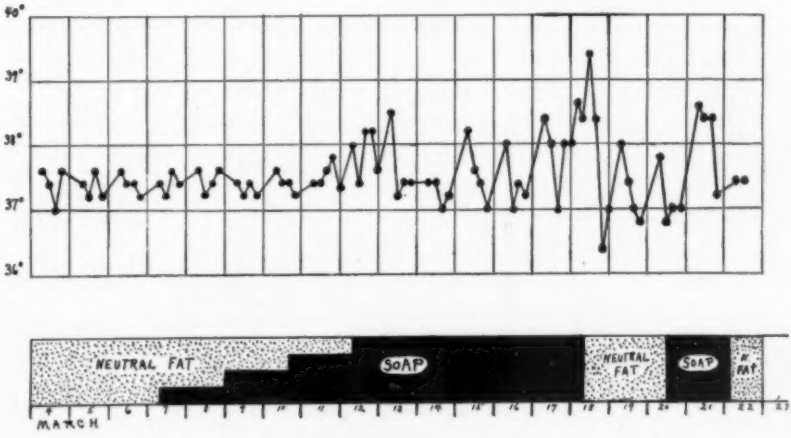

Chart 4.—Twin W. S—h.

TABLE XIII

OBSERVATIONS ON FEEDING SPLIT FAT

FAT FED	PERIOD	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE GM./DAY	FECAL FAT				FAT RETENTION		COMMENTS
						GM./DAY	PARTITION % N. F.	% F. F. A.	% SOAP	GM./DAY	% OF INTAKE RETAINED	
Free palmitic and stearic acid (2:1)	H—t 4	2¾	5.25	2	20.48	18.68	13.4	18.2	68.4	1.81	8.8	Severe diarrhea developed, necessitating stopping the experiment.
Sodium oleate	J. S—h 8	6	6.70	5	26.46	5.82	46.4	14.7	38.9	20.64	78.0	"Soap fever" developed. Weight stationary.
	W. S—h 9	6	5.80	5	24.53	4.36	29.4	28.1	42.5	20.17	82.2	"Soap fever," weight stationary.
	Average	*6*	*6.25*	*5*	*25.50*	*5.09*	*37.9*	*21.4*	*40.7*	*20.41*	*80.1*	

TABLE XIV

THE RETENTION OF ESTERS*

FAT FED	PERIOD	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE GM./KG.	FECAL FAT				FAT RETENTION		ACETONE IN URINE
						GM./DAY	PARTITION			GM./KG.	% OF INTAKE RETAINED	
							% N. F.	% F. F. A.	% SOAP			
Ethyl esters of butter	W—d 2	5¾	5.70	8	35.10	19.42	47.2	23.6	29.4	15.68	44.7	
	M—r 2	4¼	4.95	8	26.00	15.76	34.0	24.6	41.4	10.24	39.4	
	M—r 4	5¼	5.40	6	31.00	16.74	38.9	18.1	43.0	14.26	46.0	
	McK—a 2	8	6.03	8	30.00	15.54	24.8	26.2	49.0	14.46	48.2	
	Average	5¾	*5.52*	7½	*30.53*	*16.87*	*36.2*	*23.1*	*40.7*	*13.66*	*44.6*	
Ethyl esters of butter fed at a high level	M—r† 3	5	5.00	6	76.30	59.10	81.0	13.6	5.4	17.20	22.5	++
	McK—a‡ 5	9¾	6.70	2	93.40	52.22	81.4	14.2	4.4	41.18	44.1	+++
	Average	7½	*5.85*	*4*	*84.85*	*55 60*	*81.2*	*13.9*	*4.9*	*29.19*	*33.3*	

*Observations on the retention of ethyl esters of margaric acid are included in Table XII.

†Ketogenic diet, Woodyatt ratio—2.5; child lost weight.

‡Ketogenic diet, Woodyatt ratio—3 2; child lost weight. Since only a small fraction of the fat of these diets was absorbed, it appears that ketogenesis took place at a far lower level of fat retention than would be expected on diets in which the fat was supplied as triglycerides.

ethyl esters were fed, triglycerides appeared in the chyle. Interest in the ethyl esters revived during the Great War with the possibility that they might be substituted for triglycerides as foods, the glycerin of natural fats being needed in the manufacture of munitions. Lyman[47] found that dogs absorbed only a trifle over 50 per cent of ethyl palmitate in contrast to tripalmitin and natural fats, which were more than 90 per cent absorbed. Müller and Murschhauser[50] working with dogs found that the ethyl esters of lard were less well absorbed (about 75 per cent) than the natural fat (91 per cent to 94 per cent). They studied the respiratory quotient and found evidence that the ethyl esters were burned, but they hesitated to recommend their complete substitution for natural fats because of their specific dynamic action. Cox[51] recently fed ethyl esters to rats and found that growth curves on the esters of lard and of cocoanut oil were almost as good as those obtained with the natural fats. Difficulty of absorption was noted only with the longer chains (ethyl palmitate and ethyl stearate) when pure esters were fed.

Our own observations were made with the ethyl esters of butter fat. The three infants who were studied on this diet continued to thrive and gain weight normally throughout the period of this feeding (see page 429). Only when the stools were dried did it become apparent that a large part of the ester had not been utilized, for the stools contained large quantities of fat. Table XIV shows the very incomplete retention of the ethyl esters in contrast to control periods upon butter fat. The greater part of the difficulty appears to lie in the incomplete splitting of the ethyl esters.

These findings, together with the observation that ketosis occurs at a lower level of fat retention on ethyl ester diets, indicate that ethyl esters are certainly inferior to triglycerides as human foods and confirm the conclusion reached from animal studies.

H. *A Comparison of Various Natural Fats and Proprietary Fat Mixtures Designed Especially for Infant Feeding.*—In the course of our work we have studied seventeen different even carbon fats: four animal fats, six vegetable fats, and seven fat mixtures, five of which were from proprietary preparations.* Some of these experiments have been reported in the foregoing tables; the remainder are presented in Tables XV and XVI.

In Table XVII are summarized our experiments on different fats. The relation between retention and the composition of the fat is shown

*Several of these proprietary foods contain special features other than the fat mixture. These features we have not investigated, our studies being confined to the fat of the preparations: in some instances (S. M. A., Similac and Recolac) the fat was supplied us directly by the manufacturers; in others (Almata, New Zealand cream) it was extracted from the finished product by ether and rectified with petroleum ether.

in Table XVIII. The fats are arranged in order of completeness of retention as nearly as this could be determined* from our data. It is apparent that no single factor in the composition of the fat can be taken as an index of retention; the composition as a whole must be considered. Fats with the highest percentage of unsaturated acids head the list, but among those with a lower proportion of unsaturated acids, it makes a considerable difference whether the saturated acids are predominantly short, medium, or long chain acids. The saturated acids containing 14 carbon atoms or less make for good absorption, though they do not seem to be the equal of the unsaturated acids, for cocoanut oil is distinctly inferior to olive oil. Palmitic acid is only slightly less desirable than the shorter ones, whereas stearic and the longer chain acids make for poor absorption. In another section we have presented evidence that individual fatty acids are selectively absorbed when a mixed fat is fed. On the assumption that the various acids are retained to the following extent:

Unsaturated acids	98%
Short chain saturated acids	90%
Palmitic acid	88%
Stearic acid	60%
Saturated acids longer than stearic	40%,

we have calculated the expected retention for the series of fats studied. The retention so calculated is given in the last column of Table XVIII and is found to agree well with that actually observed. The one exception is the palmitin-stearin mixture; perhaps these difficultly absorbed fatty acids are more readily taken up in mixtures containing unsaturated or short chain acids than when they are present alone.

The composition as given in the table does not tell the whole story, for within the various groups of fatty acids which are tabulated the individual members doubtless show slight differences in ease of absorption. The data in the table illustrate the fallacy of imitating particular fats on the basis of determinations of a few selected constants, rather than on a complete analysis of the fatty acids. For example, in S. M. A. fat considerable pains were taken to duplicate the iodine value and saponification value believed to be characteristic of breast milk fat. It appears, however, that the percentage of unsaturated acids fell well below the mark, a fact which would at once have become apparent if determinations of the thiocyanogen value had been

*In arranging these fats in Table XVIII we have not been guided exclusively by the *average* retention figure. Some of our subjects were better fat absorbers than others, and, since it was not possible to make all comparisons on the same infants, we have taken into consideration the retention of a particular subject on the experimental fat diet as compared with a control period on butter fat.

TABLE XV

THE RETENTION OF VARIOUS ANIMAL AND VEGETABLE FATS

FAT FED	PERIOD	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE GM./DAY	FECAL FAT				FAT RETENTION	
						GM./DAY	PARTITION % N. F.	% F. F. A.	% SOAP	GM./DAY	% OF INTAKE RETAINED
Goat's milk fat	S—l 2	9½	6.60	5	32.80	1.66	9.7	27.8	62.5	30.14	91.9
	W—d 6	10	8.13	5	36.28	2.38	15.3	21.8	62.9	33.90	93.4
	Average	*9¾*	*7.37*	*5*	*34.54*	*2.02*	*12.5*	*24.8*	*62.7*	*32.02*	*92.7*
Human body fat	K. J—n 9	5	6.55	6	25.00	1.77	18.2	41.1	40.7	23.23	92.9
	F—r 11	5	5.13	6	18.85	1.16	20.5	18.9	60.6	17.69	93.8
	Average	*5*	*5.84*	*6*	*21.93*	*1.47*	*19.4*	*30.0*	*50.6*	*20.46*	*93.4*
Corn oil	H—t 8	5½	6.40	6	29.78	0.92	46.5	13.5	40.1	28.86	96.9
	G—n 4	3	3.97	6	21.99	0.87	23.0	32.9	44.1	21.11	96.0
	H—r 2	1	2.78	6	11.77	0.52	40.7	21.6	37.7	11.24	95.5
	H—k 2	5½	4.40	6	22.65	0.76	39.4	35.2	25.4	21.89	96.7
Olive oil	W. S—h 8	5½	5.50	6	27.24	2.14	48.0	22.2	29.8	25.10	92.1
	Average	*5¾*	*4.16*	*6*	*20.91*	*1.07*	*37.8*	*28.0*	*34.2*	*19.84*	*95.1*
Soy bean oil	W. S—h 5	4	4.45	6	21.25	1.01	27.5	29.6	42.9	20.24	95.2
	H—r 3	3½	4.20	6	20.51	1.60	39.3	20.1	40.6	18.92	92.2
	Average	*3¾*	*4.33*	*6*	*20.88*	*1.30*	*33.4*	*24.9*	*41.7*	*19.58*	*93.7*

TABLE XVI

THE RETENTION OF PROPRIETARY FAT MIXTURES DESIGNED FOR INFANT FEEDING

FAT FED	PERIOD	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE GM./DAY	FECAL FAT				FAT RETENTION	
						GM./DAY	PARTITION			GM./DAY	% OF INTAKE RETAINED
							% N. F.	% F. F. A.	% SOAP		
S. M. A. fat	K. J—n* 1	2¾	4.20	6	22.20	8.03	20.5	26.9	52.6	14.17	63.8
	K. J—n 2	3	4.60	6	23.40	4.10	5.9	11.0	83.1	19.30	82.5
	K. J—n 15	6¾	7.85	6	31.20	4.34	5.2	12.8	82.0	26.86	86.1
	M—r 5	5½	5.80	6	30.40	5.59	9.1	15.0	75.9	24.81	81.6
	M—r 6	5¾	6.15	6	31.70	3.55	8.7	17.3	74.0	28.15	88.8
	F—r 4	3	3.80	6	23.40	2.60	7.0	10.7	82.3	20.80	88.9
	S—l 4	9¾	6.65	6	29.70	3.11	8.3	24.0	67.7	26.59	89.5
	J. J—n 4	6¾	8.65	6	35.90	3.68	8.9	26.5	64.6	32.22	89.7
	W—d 8	10¼	8.35	5	36.60	5.79	4.7	16.7	78.6	30.81	84.2
	Average (excluding period K. J—n 1)	6¼	*6.48*	6	*30.29*	*4.10*	*7.2*	*16.8*	*76.0*	*26.19*	*86.3*
Similac fat	K. J—n 3	3¼	4.85	6	23.81	2.08	11.3	26.2	62.5	21.73	91.3
	M—r 7	6¼	6.40	6	29.30	2.30	10.7	15.4	73.7	27.00	92.2
	F—r 5	3½	4.00	6	21.00	1.17	22.7	27.6	49.7	19.83	94.4
	Average	4¼	*5.08*	6	*24.70*	*1.85*	*14.9*	*23.1*	*62.0*	*22.85*	*92.6*
Recolac fat	K. J—n 6	4¼	5.75	6	25.10	1.62	9.1	19.8	71.1	23.48	93.5
	M—r 10	7	7.30	5	28.72	2.81	7.2	10.0	82.8	25.91	90.2
	F—r 8	4¼	4.55	6	19.21	1.57	9.0	12.4	78.6	17.64	91.8
	Average	5¼	*5.87*	5¾	*24.34*	*2.00*	*8.4*	*14.1*	*77.5*	*22.34*	*91.8*
Almata fat	K. J—n 8	4¾	6.03	6	25.71	2.85	15.7	12.0	72.3	22.86	88.9
	M—r 12	7½	7.75	6	28.30	1.96	20.8	11.9	67.3	26.34	93.1
	F—r 10	4¾	4.99	6	19.70	1.41	21.5	13.5	65.0	18.29	92.8
	Average	5¾	*6.26*	6	*24.57*	*2.07*	*19.3*	*12.5*	*68.2*	*22.50*	*91.6*
New Zealand cream	K. J—n 7	4½	6.05	6	25.90	1.34	20.4	20.5	59.1	24.56	94.8
	M—r 11	7¼	7.50	6	29.31	2.24	12.6	11.0	76.4	27.07	92.4
	F—r 9	4½	4.75	6	20.30	1.58	26.6	19.8	53.6	18.72	92.1
	Average	5½	*6.10*	6	*25.17*	*1.72*	*19.9*	*17.1*	*63.0*	*23.45*	*93.1*
Butter controls	*Average*†	4½	*5.35*	6¼	*24.18*	*1.93*	*14.1*	*14.7*	*71.3*	*22.25*	*92.0*

*S. M. A. fat started one day before. Refusal and failure to gain first three days.

†An average of butter fat periods on subjects K. J—n, M—r, and F—r, each subject being given equal weight.

TABLE

SUMMARY OF EXPERIMENTS IN WHICH THE

FAT FED	NUMBER OF EXPERIMENTS AVERAGED	TABLE NO.	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE GM./DAY	DRIED STOOL	
							GM./DAY	% FAT IN
Olein	2	12*	6	6.53	4	26.05	4.49	14.2
Olive oil	4	16	3¾	4.16	6	20.91	4.98	20.5
Soy bean oil	2	16	3¾	4.33	6	20.88	5.22	25.4
Human body fat	2	16	5	5.84	6	21.93	7.34	20.0
Breast milk fat	7	3	5	6.12	6	24.89	7.57	23.8
New Zealand cream	3	17	5½	6.10	6	25.17	6.89	25.2
Goat's milk fat	2	16	9½	7.37	5	34.54	8.76	23.2
Similac	3	17	4¼	5.08	6	24.70	7.26	25.6
Recolac	3	17	5¼	5.87	5¾	24.34	7.12	28.5
Almata	3	17	5¾	6.26	6	24.57	6.53	31.1
Corn oil—butter	2	12*	6	6.40	4½	24.65	7.63	30.1
Butter	35	2	4¾	5.49	5½	25.99	8.17	35.2
Cocoanut oil	3	10	7	6.52	7	28.03	10.29	26.9
S. M. A.	8	17	6¼	6.48	6	30.29	11.45	35.9
Argo	2	11	6	7.43	6	32.90	14.69	38.2
Tripalmitin-tristearin	3	10	7½	6.94	5	30.55	21.36	55.2
Fat free	5	18	5½	5.96	4	1.06	10.62	4.8
High fat diets: Butter	5	18	7	5.96	3½	67.12	5.22	57.6
High fat diets: Goat's milk fat	5	18	7	6.01	3¼	65.87	4.74	51.1
High fat diets: Human fat	2	18	8¼	7.15	3	68.85	3.96	62.5
High fat diets: Soy bean oil	2	18	7½	6.55	3	62.51	3.79	51.0
High fat diets: Ethyl esters of butter	2	15	7½	5.85	4	84.85	69.28	80.5
Ethyl esters of butter	4	15	5¾	5.52	7½	30.53	23.38	73.1
Ethyl esters of C_{17}	2	13	10	7.00	3	39.00	40.60	70.3
Sodium oleate	2	14	6	6.25	5	25.50	11.52	44.0
High Reichert-Meissl fat	4	9	6¼	6.62	5¾	30.14	10.46	31.5
High ash butter	3	3	6¼	6.37	6⅖	26.41	12.83	36.8
Low ash butter	2	3	3½	5.44	6½	27.56	5.51	26.5
Low ash breast milk fat	2	3	4	5.40	8	24.61	2.83	26.1

*Experiments on twins not included.
†Based on two experiments only.
‡Based on four experiments only.

made. Similarly, if the saturated esters from S. M. A. fat had been fractionated, the relatively high proportion of stearic acid would have been discovered. Failure to observe these precautions resulted in a fat mixture which was not only inferior to breast milk fat but was not even as well absorbed as the butter fat it was designed to replace.

The other fat mixtures designed for infant feeding appear to have slight, if any, advantage over butter fat, with the possible exception of New Zealand cream, which gave figures a trifle higher than the others and which contains a higher proportion of unsaturated acids. This fat, the chief ingredient of which is peanut oil, is unique in containing appreciable quantities of the 20-carbon arachidic and the 24-carbon lignoceric acids. Although clinical experiences with peanut oil appear to have been favorable, evidence from experimental animals[60] suggests that these long chain acids may not be readily disposed

XVII

FAT AND OTHER FEATURES WERE VARIED

FECAL FAT							FAT RETENTION	
	PARTITION							
GM./DAY	GM. PER DAY			PER CENT			GM./DAY	% OF INTAKE RETAINED
	N. F.	F. F. A.	SOAP	N. F.	F. F. A.	SOAP		
0.64	0.22	0.17	0.25	37.5	25.2	37.3	25.41	97.5
1.07	0.43	0.29	0.35	37.8	28.0	34.2	19.84	95.1
1.30	0.46	0.31	0.54	33.4	24.9	41.7	19.58	93.7
1.47	0.28	0.48	0.72	19.4	30.0	50.6	20.46	93.4
1.85	0.23	0.59	1.03	13.1	33.9	52.9	23.04	92.4
1.72	0.32	0.28	1.12	19.9	17.1	63.0	23.45	93.1
2.02	0.26	0.49	1.27	12.5	24.8	62.7	32.02	92.7
1.85	0.25	0.40	1.19	14.9	23.1	62.0	22.85	92.6
2.00	0.16	0.26	1.57	8.4	14.1	77.5	22.34	91.8
2.07	0.39	0.25	1.43	19.3	12.5	68.2	22.50	91.6
2.43	0.53	0.96	0.95	21.8	38.6	39.6	21.73	90.6
2.88	0.25	0.54	2.09	9.5	18.1	72.4	23.10	88.9
2.84	0.14	0.90	1.80	5.2	32.4	62.4	25.19	88.7
4.10	0.29	0.68	3.13	7.2	16.8	76.0	26.19	86.3
5.67	0.62	1.14	3.86	11.8	19.4	68.8	27.23	83.0
11.77	1.27	4.22	6.28	9.9	36.0	54.1	18.78	61.5
0.51	0.07	0.06	0.37	16.2	12.5	71.4	0.55	51.7
3.01	0.46	0.25†	2.13†	14.8	9.3†	78.1†	64.11	95.5
2.43	0.29‡	0.42‡	1.58‡	12.5‡	18.2‡	71.9‡	63.44	96.3
2.49	0.39	2.11		16.0	84.0		66.36	96.4
1.93	0.85	1.09		43.2	56.8		60.58	96.9
55.66	45.19	7.73	2.75	81.2	13.9	4.9	29.19	33.3
16.87	6.21	3.89	6.76	36.2	23.1	40.7	13.66	44.6
28.54	7.14	8.70	12.70	25.0	30.5	44.5	10.46	26.8
5.09	1.99	1.05	2.05	37.9	21.4	40.7	20.41	80.1
3.23	0.25	0.70	2.28	7.8	21.8	70.5	26.91	89.0
4.74	0.29	1.12	3.29	6.7	25.0	68.3	21.66	81.7
1.46	0.17	0.68	0.62	11.3	48.0	40.8	26.10	94.8
0.71	0.12	0.32	0.27	17.7	43.8	38.6	23.91	97.1

of by the body and may accumulate in the liver, a fact which leads one to question the advisability of giving a diet rich in peanut oil for a prolonged period of time.

From the point of view of retention, none of the natural fats and fat mixtures studied yielded such high figures as did olive oil and soy bean oil. These figures were exceeded only in the two experiments in which pure olein was fed.

We do not wish to lay too much emphasis on the order in which these fats have been placed in the table. Because of the large number of fats studied, the number of observations on particular fats was often small, and it is not improbable that a larger series of experiments would shift the position of one or another of these fats to some extent. To extend our observations sufficiently to permit a rigorous statistical comparison seemed to us an unprofitable task, for we felt that the data obtained had answered several questions. They showed with sufficient clearness that all fats were not alike; that ease of absorption

TABLE XVIII

RELATION BETWEEN RETENTION AND COMPOSITION OF FAT

FAT FED	COMPONENT FATTY ACIDS (%)*					PER CENT RETENTION	
	UNSATURATED ACIDS	SATURATED ACIDS					
		SHORT CHAIN ACIDS	PALMITIC ACID	STEARIC ACID	LONGER CHAIN ACIDS	OBSERVED	CALCULATED
Olein	96	<1	2	1	<1	97.5	97.0
Olive oil	89	<1	8	3	<1	95.1	96.0
Soy bean oil	88	<1	7	5	<1	93.7	95.1
Human body fat	67	8	20	5	<1	93.4	93.5
Breast milk fat	55	6	29	10	<1	92.4	91.1
New Zealand cream	77	5	8	5	5	93.1	91.8
Goat's milk fat	36	34	19	11	<1	92.7	89.2
Similac	33	47	14	6	<1	92.6	90.5
Recolac	35	43	15	7	<1	91.8	90.4
Almata	52	26	12	10	<1	91.6	91.0
Corn oil—butter mixture (1:1)	58	21	13	8	<1	90.6	91.7
Butter	26	42	20	12	<1	88.9	88.1
Cocoanut oil	8	81	9	2	<1	88.7	89.8
S. M. A.	43	12	20	25	<1	86.3	85.5
Argo	54	1	8	37	<1	83.0	83.0
Palmitin-stearin (2:1)	3	1	64	32	<1	61.5	79.3

*Approximate values, compiled and computed from data in the literature.

was dependent upon chemical composition, and that neither breast milk fat nor human body fat—though superior to butter—represented the ideal in this respect, for both were surpassed by several vegetable fats. The differences in retention which we had found with most of these fats were relatively small and for the normal subject could have but little practical significance. It seemed quite possible, however, that in subjects with difficulty in fat assimilation, the small observed differences might prove to be large ones of considerable significance. Since we were primarily interested in these abnormal subjects, we have continued our metabolism studies upon them, attempting to confirm the differences observed in the normal subject and to see if these were accentuated. The results of this study are presented in another paper.

IV. CERTAIN PROBLEMS RELATING TO FAT ABSORPTION

A. Influence of the Quantity of Ingested Fat—Observations on Fat-Free and High Fat Diets.—For various reasons we undertook studies in which the quantity of ingested fat was varied as widely as possible. We were interested in any clinical phenomena that might appear, in the effect of fat intake upon fat retention, and, in addition, we hoped by means of fat-free diets to obtain qualitative and quantitative information as to endogenous fat excretion in infants. This last subject has been extensively studied in animals, notably by Sperry,[61] but few observations have been made in man.

Our fat-free diets were not completely devoid of fat, but the intake was reduced to approximately 1 gm. per day. They were prepared from powdered skimmed milk with added sugar. The caloric intake in these periods was reduced, but in order to supply maintenance requirements it was necessary to make some increase in the quantity of protein and carbohydrate ingested. On this diet two very definite effects were noted. Within twenty-four hours all three infants developed loose, mushy, fermentative stools. The character of the stools tended to improve on subsequent days but did not return to normal until the termination of the experimental diet. This change in the character of the stools has been noted by others,[62] but it is by no means clear whether it is due to absolute reduction of fat or to relative excess of carbohydrate in the diet.

The second phenomenon occurred in only one of the babies (H—t). This infant, shortly after the fat-free diet was instituted, developed eczema and spasmodic bronchitis. We believed this to be a mere coincidence until it was found that these symptoms cleared up when fat was added to the diet and recurred when it was again withdrawn. A further report of this case and a discussion of the relation between fat in the diet and allergic manifestations may be found in the report of Dr. M. I. Rubin.[63]

The chemical data on these periods are given in Table XIX. It is apparent that the fecal fat drops to a very low level, averaging only 0.5 gm. a day. The retention figure here has little significance, for it is probable that about four-fifths of the fecal fat consists of endogenous fat excreted into the intestine. Approximately 40 per cent of the fecal fat consisted of unsaponifiable material, having an iodine value of 66.5. The quantity of fecal fat observed under these conditions is somewhat larger than that reported by Birk[64] (from 0.17 to 0.28 gm. a day in infants) or by Parsons[65] (0.2 gm. a day in older children).

A number of our subjects were studied for short periods on ketogenic diets. All of these infants developed an abundance of ketone bodies in the urine, nor did we observe any differences in the behavior of particular fats with regard to ketogenesis if we exclude the periods on ethyl esters of butter which have been mentioned above (Table XIV). In collaboration with Dr. H. W. Josephs, studies were also made of the urobilin output in the stools; these are reported in detail elsewhere.[66] It was found that these ketogenic diets led to a definite increase in the stool urobilin, but differences in the behavior of particular fats were not encountered.

The determinations of the fat balance (Table XIX) show that the percentage retention is somewhat better than on the periods of nor-

TABLE XIX

FAT RETENTION ON FAT-FREE AND HIGH FAT DIETS

TYPE OF DIET	FAT FED	PERIOD	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE GM./DAY	FECAL FAT				FAT RETENTION		COMMENTS
							GM./DAY	PARTITION % N. F.	PARTITION % F. F. A.	PARTITION % SOAP	GM./DAY	% INTAKE RETAINED	
Fat-free	———	H—t 9	5¾	6.80	7	1.17	0.63	22.4	15.5	62.1	0.54	46.3	Developed eczema and asthma.
		G—n 10	6	4.40	2	0.98	0.58	18.4	2.8	78.9	0.40	40.5	
		G—n 11	6½	4.40	4	0.99	0.41	12.2	13.5	74.3	0.58	58.5	
		K—n 11	4½	7.05	2	1.08	0.43	11.6	14.3	74.1	0.65	60.2	
		K—n 12	4½	7.15	4	1.08	0.51	16.2	16.2	67.5	0.57	52.8	
		Average	*5½*	*5.96*	*4*	*1.06*	*0.51*	*16.2*	*12.5*	*71.4*	*0.55*	*51.7*	
	Butter	McK—n 3	9	6.30	6	76.75	3.25	14.0	8.2	77.8	73.50	95.8	
		W. S—h 11	7	6.30	3	71.25	3.40	15.3	84.7		67.85	95.2	
		J. S—h 10	7	6.20	3	67.29	4.02	17.3	82.7		63.27	94.0	
		H—k 5	6½	5.30	3	60.80	2.20	15.9	84.1		58.60	96.4	
		H—r 9	6	5.72	3	59.52	2.20	11.3	10.3	78.4	57.32	96.3	Discharge from ears.
		Average	*7*	*5.96*	*3½*	*67.12*	*3.01*	*14.8*	*9.3**	*78.1**	*64.11*	*95.5*	
High fat (low ash) diet	Goat's milk fat	J. S—h 9	6½	5.75	3	63.92	2.14	10.8	18.1	71.1	61.78	96.7	Otitis, discharging.
		W. S—h 10	6½	5.78	3	67.37	2.61	12.8	20.2	67.1	64.76	96.1	
		H—k 4	6	5.00	3	56.40	2.71	13.1	16.4	70.6	53.69	95.2	
		H—r 8	5½	5.40	3	55.77	1.65	13.3	18.1	68.8	54.12	97.0	Discharge from ears.
		W—d 7B	10	8.10	4	85.89	3.06				82.83	96.4	
		Average	*7*	*6.01*	*3½*	*65.87*	*2.43*	*12.5†*	*15.7†*	*71.9†*	*63.44*	*96.3*	
	Human body fat	J. S—h 11	8¼	7.10	3	67.50	1.81	17.4	82.6		65.69	97.3	Otitis, discharging.
		W. S—h 12	8¼	7.20	3	70.20	3.17	14.6	85.4		67.03	95.5	
		Average	*8¼*	*7.15*	*3*	*68.85*	*2.49*	*16.0*	*84.0*		*66.36*	*96.4*	
	Soy bean oil	H—k 6	7¾	6.50	3	63.76	2.52	45.4	54.6		61.24	96.0	
		H—r 10	7¼	6.60	3	61.26	1.34	41.0	59.0		59.92	97.8	
		Average	*7½*	*6.55*	*3*	*62.51*	*1.93*	*43.2*	*56.8*		*60.58*	*96.9*	
	Olive oil	J. S—h 12	8½	7.54	2	70.04	1.98	48.5	51.5		68.06	97.2	
	Corn oil	W. S—h 13	8½	7.57	3	57.12	2.52	60.2	39.8		54.60	95.6	

*Average of two experiments only.
†Average of four experiments only.

mal fat intake; moreover, the differences in the behavior of individual fats are practically wiped out. We are inclined to attribute this improved retention on the high fat diets to the lower mineral intake. Comparisons of high and normal butter fat periods made under conditions in which the mineral intakes were similar show little difference in the percentage retention.* This question is further discussed in the following section.

B. *The Relation Between the Dried Weight of the Feces, the Fecal Fat, and Fat Absorption.*—In the foregoing discussions of our results, we have gone on the assumption that, barring conditions of low fat intake, the most significant measure of fat absorption is the percentage of the fat intake retained. In this we have followed the majority of workers in the field. The correctness of this point of view has, however, been challenged, particularly by H. S. Hutchison,[67] and, since his views have met with some acceptance, a defense of our procedure would seem to be in order.

Hutchison observed in normal subjects, and individuals in certain pathologic states as well, that the percentage of fat in the dried feces was singularly constant, being approximately one-third of the dried fecal weight. Despite the fact that quite different percentages of fat had been found in the feces of dogs and rats, he concluded that this percentage of fat was physiologic for human feces and raised the question of the possible functions of fecal fat. He conceded that impaired ability of the intestine to absorb fat would result in an increased percentage of fat in the feces, an increased quantity of fecal fat, and low percentage retention, but he maintained that the converse was not true: an increased quantity of fecal fat and consequent low percentage retention did not necessarily imply difficulty in absorption.

He described a state, due to atony of the bowel or to other causes unrelated to fat absorption, in which the pathologic process led to increased bulk of the feces; fat would then be diverted to the feces in order to maintain the physiologic percentage, even though the intestine had in no way lost its ability to absorb fat. In such a condition the percentage retention would be low although the ability of the intestine to absorb fat had not suffered; the clue to this situation would be given by the fact that the percentage of fat in the stool failed to increase. From these premises it follows that the percentage of fat in the feces is a more valuable criterion of absorption than the percentage retention.

A second point made by Hutchison to show that the percentage retention is not the significant criterion of absorption concerns the effect

†Average of four experiments only.

*In a preliminary communication (Proc. Third Internat. Paediat. Congress, Acta paediat. 16: 165. 1933) we stated our impression that the percentage absorption tended to diminish as the quantity of ingested fat was increased. Further observations, particularly those on high fat diets, have failed to sustain this view, which we now wish to retract.

of varying fat intake on fat retention.* When he arranged his normal cases with liberal fat intake in order of the amount of fat ingested, it appeared that the fecal fat tended to remain constant regardless of the intake, whereas, if the percentage retention were the criterion of normal absorption, an increase in the intake would have been followed by an increase in the fecal fat.

The points made by Hutchison are well taken, and his arguments appear to be convincing. Nevertheless, we believe that his data are susceptible of a different interpretation, one which is in better harmony with our own results.

In the first place, we believe that the available data, taken as a whole, do not justify the conclusion that the percentage of fecal fat tends to approach a physiologic norm. Normal subjects under standard conditions show wide fluctuations in the percentage of fecal fat. Even in Hutchison's own data such variations are found; in his normal infants the fecal fat varied between 20.7 per cent and 46.0 per cent; in his series of atrophic infants it varied between 23.4 per cent and 47.8 per cent; in subjects with tetany it was between 25.0 per cent and 51.0 per cent; and in those with uncomplicated rickets the extremes were 18.6 per cent and 52.9 per cent. It thus appears that little reliance can be placed on the percentage of fat in the individual case, even if the average value were relatively constant. Our own data (Table XVII) show, however, that the average value for the percentage of fecal fat is a constant only when butter is fed. With the more readily absorbable fats it falls, and with the less readily assimilable fats it rises consistently. Moreover, even on butter the percentage of fat in the feces fails to remain constant when significant changes are made in the composition of the diet. We are inclined to attribute the constancy of the figure which Hutchison and others obtained to the fact that such observations were made under relatively constant conditions. Hutchison made no attempt to test out his theory by producing independent variations in the fat and other constituents of the feces. Such variations were produced in our experiments on fat-poor and on ketogenic diets. Compared with normal periods, our fat-poor diets were richer in mineral, a factor which served to increase the bulk of the dried stool. According to Hutchinson, this should have resulted in an increase in the fecal fat. No such effect, however, was noted. On the contrary the absolute amount of fat in the feces fell sharply, and the percentage of fecal fat fell well below what Hutchison regarded as characteristic for the human species. Similar results were obtained by Holt and Fales[62] with diets from which fat was less rigidly

*As we have pointed out above, we agree with Hutchison that the retention percentage is an inaccurate guide to absorption when the fat intake is low.

excluded, their subjects receiving 5.0 to 7.0 gm. of fat a day. In their experiments the total ash and the total solids of the stool were increased, and yet a sharp reduction occurred in the fecal fat. The absolute quantity was diminished, and the fecal fat constituted less than 10 per cent of the dried feces.

The converse experiment we carried out in the periods on ketogenic diets. In order to avoid overfeeding these infants the dietary constituents other than fat were reduced. The mineral content of the diet was somewhat less than half that of the normal periods, being comparable to that in our low ash diets. The total solids of the feces fell below normal, and from Hutchison's thesis one would have expected a reduction in the fecal fat. However, no such reduction occurred. The percentage of fat in the feces increased to well above 50 per cent, and, if we contrast these periods with our low ash periods in which butter was fed at the normal level, it appears that the absolute quantity of fecal fat was increased on the high fat diet. The percentage retention on the low ash periods is almost identical regardless of whether butter was fed at the normal level or at the ketogenic level. In the former case the average retention was 94.8 per cent whereas the average retention on high butter fat periods was 95.5 per cent. Unfortunately these experiments were not carried out on the same subjects. Possibly the slightly better retention percentage on the high fat periods was due to the fact that the infants were older. At least our data fail to confirm the view that the percentage of fat in the feces is constant for the species. The variations produced by diet suggest that the differences found between man, the dog, and the rat may also find their explanation in differences in diet. The retention percentage on the other hand appears to hold regardless of whether the fat intake is normal or high, although it fails one on low fat diets because the endogenous fat excretion then comprises a large part of the fecal fat.

As regards Hutchison's second point, the relatively constant fecal fat in the presence of increasing fat intake, his data are unfortunately not given in sufficient detail to permit one to criticize them with certainty, but other explanations of this finding are possible. If his periods on high and low fat had been done in the same infants and within a short space of time, failure to find an increase in the fecal fat on the high fat intake would have been much more significant. On the other hand, if (as may well be the case from the information furnished) the periods on lower fat intake were in young infants and those receiving from 30 to 40 gm. a day were in older infants, the results may be explained on the basis that the older infants were more efficient fat absorbers. We ourselves have obtained evidence that fat

absorption is affected to some extent by age. In premature infants and in full-term twins fat absorption is very imperfect. To a less extent we have found this to be true of normal infants during the early weeks of life. In such subjects we have found the percentage of retention with butter fat to be nearer 80 per cent than 90 per cent, and the proportion of fat in the dried feces is nearer 1:2 than 1:3; hence even if we use Hutchison's measuring stick, these young infants appear to absorb fat imperfectly. Just when this state of affairs is outgrown is not easy to say. It may be that at the age of ten or twelve weeks fat absorption is as perfect as it ever will be; on the other hand, it may be that as the infant grows older his absorption improves—rapidly during the early weeks and more slowly thereafter, reaching the absolute maximum only in the latter part of the first year. This latter possibility would easily explain Hutchison's results. It is unfortunate that he did not record the ages of his patients. Our results, presented in Table XX, are compatible with the view that absorption is a function of age during the early months of life. In conclusion we feel that no adequate reason has, as yet, been adduced for abandoning the retention percentage as an index of fat absorption.

TABLE XX

RELATION BETWEEN AGE AND FAT RETENTION*

AGE GROUP	NUMBER OF OBSERVATIONS AVERAGED	PER CENT OF FAT IN DRIED FECES (AVERAGE)	PER CENT OF FAT INTAKE RETAINED (AVERAGE)
0-1 month	3	46.0	84.2
1-2 months	6	40.5	84.6
2-3 months	6	34.6	86.8
3-4 months	7	30.2	89.6
4-5 months	(1)	(44.0)	(84.8)
5-6 months	11	30.9	90.5
6-7 months	6	33.2	90.4
7-8 months	(1)	(36.6)	(91.7)
8-9 months	0	----	----
9-10 months	(1)	(38.3)	(87.3)

*This table includes all periods on normal, full-term infants fed on butter fat, skimmed cow's milk, and some form of sugar. Periods on premature infants and twins are not included even if these infants had apparently overcome their early handicap, for it seemed doubtful whether they could fairly be compared with full-term, normal infants of the same age.

Although it is somewhat beside the present point, it may be well to point out that Hutchison's conclusions in regard to fat absorption in atrophic infants are no firmer than the premises on which they are based. Hutchison found, like others, that the percentage retention in these infants was somewhat low (average 76.5 per cent in twenty-two subjects), but he maintained that this was not due to impaired fat absorption. He attributed it to (1) a comparatively low fat intake and (2) an increase in the bulk of the feces, causing diversion of fat

to maintain the physiologic percentage in the feces. As we have pointed out, the latter contention does not seem to be well founded. As to the former, although we agree that a low fat diet will lead to a low percentage retention, we do not agree that such a slight reduction in the intake (e.g., to 17.6 gm. a day) could diminish the percentage retention to the extent observed. It would probably require an intake as low as 5 gm. a day to do this; in fact, Holt and Fales[62] in four periods on normal subjects reported an average retention of 76.85 per cent with an average intake of 5.5 gm. of fat a day. We have five periods on normal infants who received quantities of fat analogous to those given by Hutchison to his atrophic infants and who retained distinctly more of their fat. These subjects received 14.2 to 19.4 gm. of fat a day (average 16.9 grams) and retained from 79.5 per cent to 90.9 per cent (average 85.1 per cent). It thus appears that the low fat retention in Hutchison's atrophic infants is not adequately explained by the low intake, making it necessary to return to the earlier view that these infants have a certain amount of difficulty in absorbing fat.

C. *The Selective Absorption of Individual Fatty Acids.*—In preceding sections we have shown that the character of the fatty acids which compose a particular fat determine the extent to which it is absorbed. However, it does not follow from this that there is selective absorption of individual fatty acids in a mixed fat. It is conceivable that the more readily absorbable fatty acids act as a leaven, facilitating the absorption of all that are present. The question is largely one of academic interest, but, since it has been the subject of controversy,[68] we shall present the evidence we have which bears upon it.

It has been generally found[65, 69] that the fecal lipids are more saturated than those of the food. We ourselves have found this to be the case as the data in the accompanying graph (Chart 5) bear witness. This, however, does not necessarily mean selective absorption of unsaturated fatty acids for it is also possible (1) that unabsorbed unsaturated fatty acids may become hydrogenated during passage through the intestine and (2) that the lower iodine value of the fecal fat may be due to admixture with a more saturated endogenous fat excreted by the intestine. This latter possibility we have attempted to rule out by making a correction in the value of our fecal fat for endogenous fat excretion, based on the assumption that the endogenous fat excretion is not materially different on diets containing fat than it was found to be on our fat-free diets. By deducting from the total fecal fat this assumed value for endogenous fat excretion, we obtain a value for the unabsorbed food fat; this we have plotted on the graph as the "corrected" fecal fat. An examination of Chart 5 shows that such a

correction fails to abolish the discrepancy between the iodine value of the food and of the fecal fat in the case of fats which contain an abundance of both saturated and unsaturated acids (in which selective absorption if it occurred should be conspicuous). On the other hand when we come to fats like olive oil that contain a very small percentage of saturated acids (and in which there would be little opportunity for selective absorption in any case) we find that the correction almost completely removes the discrepancy between the fecal and food fat. We can thus conclude that admixture with endogenous fat does not account for the lower iodine value of the fecal fat when mixed fats (saturated and unsaturated) are fed.

The possibility that unabsorbed unsaturated fatty acids may become saturated during passage through the intestine (as is known to be the

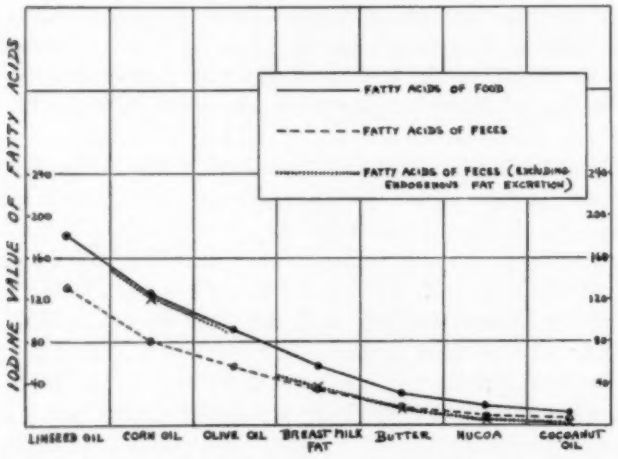

Chart 5.—Comparison of iodine values of fatty acids of food and feces.

case with sterols) was tested out in our experiments described in a foregoing section in which a comparison was made of a diet of pure olein with one of a mixture of corn oil and butter of identical iodine value. If saturation of double bonds occurred during passage through the intestine, there should be an identical lowering of the iodine value of the fecal fat in both sets of experiments. On the other hand, if there is no such saturation, the fecal residue on the olein diet should closely resemble olein in its iodine value; whereas on the corn oil-butter diet, in which selective absorption is possible, a considerable fall in the iodine value of the fecal fat might occur. The data in Table XI show the marked contrast between the two diets. On the pure olein diet the iodine value of the fecal lipids averages 71.2, being not far below that of the food fat, whereas in these same infants on

the corn oil-butter mixture the iodine value of the fecal fat fell to an average value of 52.7, a drop twice as great as that in the olein diet. It is probable that had our olein been 100 per cent pure rather than only 95 per cent pure, the fall in the iodine value of the fecal lipids would have been even less. It thus appears that saturation during passage through the intestine will account for only a small part of the drop in iodine value of the fecal lipids and that selective absorption of individual fatty acids must occur in order to explain the values actually found.

By means of determinations of the iodine value and thiocyanogen value of the food and fecal fatty acids, using the formulas given by Jamieson,[15] we have calculated the percentage of saturated acids, of oleic acid, and of linoleic acid in the food and fecal fat, and from these figures we have obtained data as to the percentage absorption of these fatty acids in a mixed fat. The data are presented in Table XXI. The error in the method is such that significant figures for linoleic acid cannot be obtained when the amount ingested is less than 1 gm. a day as was the case with diets of breast milk fat and butter; these figures are therefore not included. However, in our periods in which corn oil was given, the feeding contained 5 gm. or more of linoleic acid a day, and the calculations assume some significance. Table XXI indicates that the oleic acid fraction regularly shows a better retention than the saturated acid fraction. In four of the five periods in which the retention of linoleic acid could be calculated with some degree of accuracy, the retention of linoleic exceeded slightly that of oleic acid; in one period the reverse was the case. We do not feel justified in concluding from this that linoleic is slightly better absorbed than oleic acid; more observations would be required to establish this point. The data suggest, however, that this may be the case.

D. *The Significance of the Fat Partition in the Feces.*—It has been the general practice to express this in percentages of neutral fat, free fatty acids, and soaps with the assumption—stated or implied—that variations encountered were due to differences in fat splitting. For example Holt, Courtney, and Fales (quoted in Table I) found quite different percentages on diets of breast milk and cow's milk. Their findings are in general agreement with earlier authors and have since been confirmed by Harrison and Sheldon;[70] a diet of breast milk gives rise to a higher percentage of neutral fat and free fatty acid in the feces, whereas on cow's milk a much larger proportion of soap is found. Our own experiments, in which only the fat was varied, show similar differences between breast milk fat and butter fat. However,

TABLE XXI

RETENTION OF SATURATED AND UNSATURATED FATTY ACIDS WHEN MIXED NATURAL FATS ARE FED

FAT FED	PERIOD	INTAKE (GM./DAY)			OUTPUT IN FECES (GM./DAY)			RETENTION (GM./DAY)			RETENTION (% OF INTAKE)		
		LINOLEIC ACID	OLEIC ACID	SATURATED ACIDS	LINOLEIC ACID	OLEIC ACID	SATURATED ACIDS	LINOLEIC ACID	OLEIC ACID	SATURATED ACIDS	LINOLEIC ACID	OLEIC ACID	SATURATED ACIDS
Breast milk fat	G—n 5		9.90	6.75		0.13	0.71		9.77	6.04		98.7	89.4
	G—n 6		10.71	7.30		0.23	1.27		10.48	6.03		97.9	82.6
	K—n 5		14.69	10.02		1.02	2.39		13.67	7.63		93.1	76.1
	K—n 7		13.32	9.08		0.83	1.81		12.49	7.27		93.8	80.1
	Average		*12.16*	*8.29*		*0.55*	*1.55*		*11.60*	*6.74*		*95.9*	*82.0*
Butter fat	G—n 1		5.44	14.83		0.49	2.36		4.95	12.47		91.0	84.1
	G—n 2		5.45	14.84		0.27	2.94		5.18	11.90		95.0	80.2
	G—n 12A		6.57	17.90		0.24	1.65		6.33	16.25		96.3	90.8
	G—n 12B		6.57	17.90		0.23	1.65		6.34	16.25		96.5	90.8
	G—n 13		6.30	17.15		0.54	2.64		5.76	14.51		91.4	84.6
	K—n 1		6.65	18.10		1.17	3.06		5.48	15.04		82.4	83.1
	K—n 2		6.75	18.38		0.58	3.10		6.17	15.28		91.4	83.1
	H—t 1		7.39	20.13		0.39	2.33		7.00	17.80		94.7	88.4
	H—t 10A		6.64	18.09		0.06	0.91		6.58	17.18		99.1	95.0
	H—t 10B		6.64	18.09		0.19	1.85		6.45	16.24		97.1	89.8
	H—t 11		7.47	20.34		0.44	1.73		7.03	18.61		94.4	91.5
	Average		*6.53*	*17.80*		*0.42*	*2.20*		*6.12*	*15.59*		*93.6*	*87.3*
Low ash-breast milk fat	G—n 9		12.95	8.83		0.14	0.58		12.81	8.25		98.9	93.4
	K—n 10		15.35	10.46		0.05	0.57		15.30	9.89		99.7	94.6
Low ash-butter	K—n 9		7.76	21.15		0.08	1.52		7.68	19.63		99.0	92.8
High ash-butter	G—n 14		6.21	16.92		0.88	4.03		5.33	12.89		85.8	76.2
High volatile acids added to butter	H—t 6		5.91	16.94		0.27	3.01		5.64	13.93		95.4	82.2
	H—t 7		8.25	23.64		0.35	2.60		7.90	21.04		95.8	89.0
Olive oil	G—n 4		17.99	3.03		0.24	0.58		17.75	2.45		98.7	80.9
Corn oil	H—t 8	12.24	13.61	3.93	0.16	0.28	0.48	12.08	13.33	3.45	98.7	97.9	89.0
Corn oil and butter (twins)	J. S—h 3	5.75	7.35	6.13	0.91	0.84	2.81	4.84	6.51	3.32	84.2	88.6	54.2
	W. S—h 3	5.68	7.25	6.05	0.66	1.24	1.56	5.02	6.01	4.49	88.4	82.9	74.2
	Average	*5.72*	*7.30*	*6.09*	*0.79*	*1.04*	*2.19*	*4.93*	*6.26*	*3.91*	*86.3*	*85.8*	*64.2*
Corn oil and butter (normal subjects)	H—r 6	6.52	8.33	6.95	0.07	0.43	0.72	6.45	7.90	6.23	98.9	94.8	89.6
	K. J—n 17	8.22	10.51	8.77	0.32	1.31	2.00	7.90	9.20	6.77	96.1	87.5	77.2
	Average	*7.37*	*9.42*	*7.86*	*0.20*	*0.87*	*1.36*	*7.18*	*8.55*	*6.50*	*97.5*	*91.2*	*83.4*

if we express the fecal lipids in absolute amounts rather than in percentages, a somewhat different impression is obtained:

TABLE XXII

	PARTITION OF FECAL FAT					
	PERCENTAGE			GRAMS PER DAY		
	N. F.	F. F. A.	SOAP	N. F.	F. F. A.	SOAP
Average of 7 periods on breast milk fat	13.1	33.9	52.9	0.23	0.59	1.03
Average of 35 periods on butter fat	9.5	18.1	72.4	0.25	0.54	2.09

It then appears that the quantity of neutral fat and free fatty acid are approximately identical on the two diets and that the only difference is in the larger amount of soap in the stool on the diet of butter fat. If we examine our summarized experiments in Table XVII in which fat partition in the feces is expressed in absolute amounts as well as in percentages, we find again that there is almost no variation in the daily excretion of neutral fat until we come to the very poorly absorbed fats like the palmitin-stearin mixture and ethyl esters, and barring these there is no evidence of an inverse relation between retention and the amount of neutral fat in the stools. In other words, *incomplete fat splitting does not seem to be a factor limiting absorption until we come to these very poorly absorbed fats.* This same point is illustrated in Chart 6 in which we have plotted data from individual experiments showing the relation between fat retention and the quantities of the various fecal lipids.

There does appear to be a slight inverse relation between the free fatty acid of the stool and fat retention, but there is a very striking inverse relation between retention and the quantity of soap in the feces. It is not clear what the factor is which limits absorption under these conditions; two explanations are possible. It may be that the difficulty is primarily with the absorption of soap. On the other hand, the fact that most of the unabsorbed fatty acid is found in the feces as soap may mean only that an excess of base has been available to neutralize unabsorbed fatty acid. Some observations made by Keller[71] suggest that the latter explanation is the correct one. He made analyses of the particular bases excreted as soap in the feces and found wide fluctuations; at times the alkali soaps were in excess, and at other times the alkaline earth soaps were more abundant. These differences could not be attributed to the fat of the diet. Keller was led to the conclusion that the nature of the base combined as soap in the feces was dependent on the base available for excretion by this route at any particular time. This view was also supported by Folin and Wentworth.[72]

Inasmuch as the "neutral fat" fraction contained not only the neutral fat but also the unsaponifiable matter of the feces, we undertook to make some independent determinations of the unsaponifiable matter, as it seemed possible that the constant value of the neutral fat fraction might be due to the fact that this consisted largely of un-

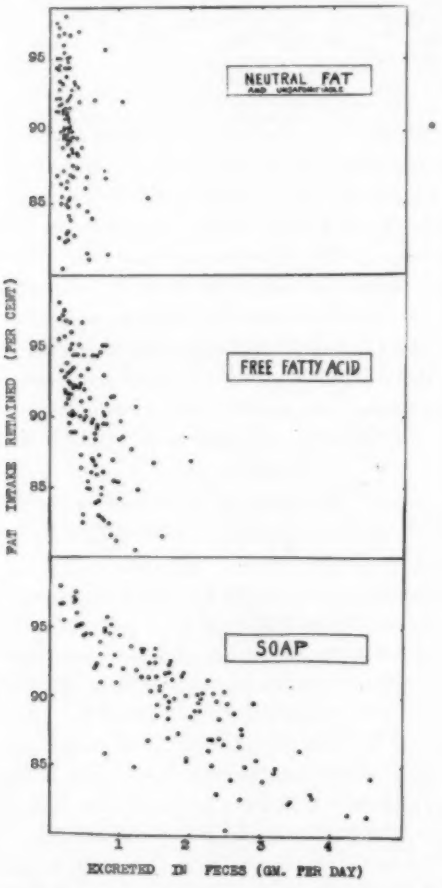

Chart 6.—Relation between fat retention and the fat partition in the feces.

saponifiable material. These determinations shown in Table XXIII indicate that the values obtained for unsaponifiable matter were, within the limits of error, identical with those we had obtained for the neutral fat fraction containing the unsaponifiable matter. In other words the feces contained no appreciable amount of neutral fat until we come to the poorly absorbed palmitin-stearin mixture, in which

incomplete fat splitting makes its appearance. The somewhat higher values for "neutral fat" in the feces on diets of some of the vegetable oils can be attributed to the fact that these oils—notably corn oil—are richer in unsaponifiable matter, which is not completely absorbed. The iodine value of the unsaponifiable matter appears to be constant with the exception of the periods on vegetable oils during which it tends to be higher. This can be attributed to the fact that the unsaponifiable matter in these oils is highly unsaturated.

TABLE XXIII

OBSERVATIONS ON UNSAPONIFIABLE MATTER OF FECES

DIET		NUMBER OF EXPERIMENTS AVERAGED	UNSAPONIFIABLE MATTER OF FECES (GM./DAY)	IODINE VALUE OF UNSAPONIFIABLE MATTER
Olive oil		1	0.25	85.3
Corn oil and olive oil		1	0.42	
Corn oil		1	0.56	
Breast milk fat	Medium ash	4	0.22	61.6
	Low ash	2	0.13	68.6
Butter	Medium ash	16	0.27	64.8
	Low ash	2	0.15	68.2
Nucoa		1	0.25	---
Cocoanut oil		2	0.20	68.8
Tripalmitin-tristearin		1	0.22	---

In view of these findings it would seem to us desirable to abandon the conventional practice of expressing the fat partition in feces in percentages and to express this in absolute amounts. Erroneous impressions in regard to fat splitting are thus less likely to occur.

Conclusions

From the above studies we feel justified in drawing the following conclusions regarding the intestinal absorption of fat by infants:

1. The size of the fat particles is without influence on fat absorption.

2. Of other food constituents that might influence fat absorption, minerals alone appear to do so, exerting an unfavorable influence. This effect is probably due to the alkaline earths.

3. Volatile fatty acids in amounts considerably larger than those present in butter appear to be harmless.

4. In a mixed fat, absorption is favored by the presence of (a) fatty acids containing one or more unsaturated linkages and (b) fatty acids with relatively short carbon chains. It is impaired by the presence of long chain saturated fatty acids. Contrary to the general belief, the melting point of a fat is not per se the factor determining absorption.

5. Certain pure odd carbon fats, when pushed to ketogenic levels, will lead to the production of ketone bodies.

6. Split fat appears to be impractical for use in diarrhea; free fatty acids are irritating to the intestine; and soaps increase the water requirements.

7. Ethyl esters are distinctly inferior to triglycerides. They appear to be split with difficulty and are retained only to a limited extent. When they are fed, ketone bodies make their appearance at an unusually low level of fat absorption.

8. A comparative study of various fats and fat mixtures indicates that those mixtures specially designed for infant feeding are no better absorbed than butter. Certain animal and vegetable fats are, however, distinctly better absorbed. The ease with which a particular fat is absorbed can be predicted, with considerable accuracy, from a knowledge of its composition.

9. Fat-poor diets tend to produce loose, fermentative stools; at times they appear to bring out allergic manifestations.

10. Fat absorption appears to be most satisfactorily measured by the percentage of ingested fat retained. This figure does not seem to be materially affected by increasing the quantity of fat in the diet, although it becomes inaccurate when the amount of ingested fat is very small since the fecal fat then consists largely of endogenous fat excretion.

11. To some extent fat absorption is affected by the age of the subject.

12. A constant relation between the total solids and the fat of the feces, such as has been claimed, does not appear to hold.

13. The claim that atrophic infants are able to absorb fat normally does not appear to be well founded.

14. Evidence is presented for the selective absorption of individual fatty acids in a mixed fat.

15. In normal subjects, fat is as a rule completely split in the intestine; the portion of the fecal fat usually reported as neutral fat actually consists of unsaponifiable material.

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STUDIES IN FAT METABOLISM

II. Fat Absorption in Premature Infants and Twins

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IN PART I of this study,[1] the article dealing with normal infants, we reported certain differences in the absorption of particular fats which appeared to depend on the nature of the constituent fatty acids. From the point of view of absorption the most desirable fatty acids were found to be those containing unsaturated linkages and, next to these, acids with relatively short carbon chains. It was not established that the presence of more than one double bond was advantageous though a little evidence pointed to that conclusion. The differences observed in normal subjects were small, but, since it seemed possible that subjects having difficulty in fat absorption might show larger differences of some practical significance, we undertook to make such comparisons in a group of poor fat absorbers.

Fat absorption is defective in a number of clinical conditions; states in which the external secretion of the pancreas or bile is excluded from the intestine, in celiac disease, in tuberculous disease with obstruction of the lacteals, to some extent in marasmic infants and in the newborn, in premature infants and twins, in certain infectious and post-infectious states, and particularly in the presence of diarrhea. Some of these conditions are rare, and others are difficult to work with since the state of the patient remains constant for a relatively short period of time. The premature group seemed to us the most promising one for comparative studies, and we therefore carried out a series of balance experiments in these subjects.

METHODS OF STUDY

The technic of the balance experiments differed somewhat from that employed with mature subjects. Infants of both sexes were used. No attempt was made to put the subjects on a frame, but the feces were collected in diapers of absorbent cotton. The soiled portions of these diapers were carefully removed and placed in an enlarged Soxhlet apparatus where they were extracted for three days first with acidified alcohol and then with ether. This extract was evaporated to

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dryness, the residue taken up in petroleum ether, and the petroleum ether extract filtered, evaporated to dryness and weighed. It was found by blank determinations that a small amount of lipid material could be extracted from the cotton itself, averaging 0.5 gm. for the quantity of cotton employed in typical experiments of five or six days' duration. This value was therefore deducted from the weight of the dried petroleum ether extract to give the actual weight of the fecal lipids for the period.

In the tables which follow, the retention figures are based on the total lipids. However, in view of the possibility that the feces of these infants might contain an unusually large proportion of unsaponifiable material—derived either from intestinal secretions or from contamination with mineral oil which was used in wiping these infants—we also made a series of determinations of the total fatty acids of the feces. It was found in more than a dozen experiments that the percentage retention of the fatty acids differed only very slightly (rarely more than 3 or 4 per cent) from that calculated for the total lipids. We therefore felt that the simpler method of determining the total lipid retention provided a sufficiently accurate measure of fat absorption for our purpose.

The experimental feedings were prepared as in our previous report[1] from skimmed milk with added sugar, in which the various fats were incorporated by homogenization.

RESULTS

In Table I are presented twenty-two experiments on healthy premature infants to whom various fats were given. Our data confirm those of other workers[2] that these infants absorb fat with difficulty. Only a trifle more than half of the butter fat intake is retained on the average, and in individual periods even less than this. However, when we come to the fats containing predominantly unsaturated fatty acids —olive oil and soy bean oil—we find that retention is much more complete; from 15 to 25 per cent more of the intake is retained. It is apparent that in these infants the difficulty in absorbing fat is such as to be a serious impediment to nutrition when ordinary milk formulas are used; this may in large measure be avoided by the substitution of a more readily absorbable fat.

Similar, though less striking, results were obtained in a pair of full-term twins (Table II). Only the smaller and feebler of these showed differences in fat retention comparable to those observed with premature infants.

It will be noted (Table I) that the retention of soy bean oil is on the average better than that of olive oil, suggesting that the presence of a second double bond is advantageous. Only a few comparisons

were, however, made in the same subjects, and it is possible that the infants studied on soy bean oil were better fat absorbers. In Table III we have collected observations made in identical subjects. It appears

TABLE I

FAT RETENTION OF PREMATURE INFANTS ON VARIOUS NATURAL FATS

FAT FED	PERIOD	AGE (MO.)	WEIGHT (KG.)	DURATION OF EXPERIMENT (DAYS)	FAT INTAKE (GM. PER DAY)	FECAL FAT (GM. PER DAY)	FAT RETENTION	
							GM. PER DAY	% OF INTAKE RETAINED
Butter	C—n, "A" 2	1½	2.02	5	11.16	4.56	6.60	59.1
	C—n, "A" 5	2	2.64	5	16.80	5.64	11.16	66.4
	C—n, "B" 1	1	1.79	5	10.44	4.90	5.54	53.1
	C—n, "B" 5	2	2.43	5	15.12	4.84	10.28	68.0
	D—t 2	¾	1.92	5	11.47	3.70	7.77	67.7
	B—r 1	1½	2.55	5	6.69	2.48	4.22	63.1
	B—r 4	2	3.25	6	21.56	11.28	10.28	47.7
	D—m 3*	1¾	3.17	3	17.99	9.29	8.70	48.4
	D—s 1	2	2.56	8	19.99	9.83	10.16	50.8
	Average	*1½*	*2.48*	*5½*	*14.58*	*6.28*	*8.30*	*58.3*
Olive oil	C—n, "A" 1	1	1.73	5	11.48	4.35	7.13	62.1
	C—n, "B" 2	1¼	2.05	5	10.60	3.45	7.15	67.5
	B—r 3	1¾	3.10	6	21.74	4.81	16.92	77.8
	D—m 2	1½	3.05	6	17.58	3.70	13.88	78.9
	K—e 1	1	2.44	5	15.84	4.01	11.83	74.7
	M—s 1	¾	2.40	6	14.04	3.71	10.34	73.6
	Average	*1¼*	*2.46*	*5½*	*15.21*	*4.01*	*11.21*	*72.4*
Soy bean oil	C—n, "A" 3	1½	2.16	5	12.94	2.27	10.66	82.5
	C—n, "A" 4	1¾	2.47	5	16.19	2.14	14.06	86.8
	C—n, "B" 3	1½	2.26	5	12.94	2.60	10.33	79.9
	C—n, "B" 4	1¾	2.49	5	15.93	3.55	12.37	77.7
	W—t 1	¾	2.15	6	12.04	1.38	10.67	88.6
	Average	*1½*	*2.31*	*5½*	*14.01*	*2.39*	*11.62*	*83.1*
Human body fat	B—r 2	1½	2.83	6	19.76	4.90	14.86	75.2
	D—m 1	1	2.75	6	17.66	4.71	12.95	73.3
	Average	*1¼*	*2.79*	*6*	*18.71*	*4.80*	*13.91*	*74.3*

*Period terminated because infection developed.

TABLE II

FAT RETENTION OF TWO FULL-TERM TWINS*

PERIOD	FAT FED	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE (GM./DAY)	FECAL FAT (GM./DAY)	FAT RETENTION	
							GM./DAY	PER CENT OF FAT INTAKE RETAINED
J. S—h 1	Butter	2¼	3.45	6	18.27	4.04	14.23	77.9
J. S—h 2	Olive oil	2½	3.73	6	18.89	2.75	16.14	85.4
W. S—h 1	Butter	2¼	3.17	6	16.92	5.72	11.20	66.2
W. S—h 2	Olive oil	2½	3.40	4	17.55	1.47	16.08	91.6

*These infants were placed on metabolism frames for the collection of excreta as described in our preceding report.[1]

TABLE III

FAT RETENTION OF INDIVIDUAL PREMATURE INFANTS IN CONSECUTIVE PERIODS

SUBJECT C—N "A"			SUBJECT C—N "B"			SUBJECT B—R			SUBJECT D—M		
AGE (MO.)	FAT FED	PER CENT FAT RETENTION	AGE (MO.)	FAT FED	PER CENT FAT RETENTION	AGE (MO.)	FAT FED	PER CENT FAT RETENTION	AGE (MO.)	FAT FED	PER CENT FAT RETENTION
1	Olive oil	62.1	1	Butter	53.1	1¼	Butter	63.1	1	Human body fat	73.3
1¼	Butter	59.1	1¼	Olive oil	67.5	1½	Human body fat	75.2	1¼	Olive oil	78.9
1½	Soy bean oil	82.5	1½	Soy bean oil	79.9						
1¾	Soy bean oil	86.8	1¾	Soy bean oil	77.7	1¾	Olive oil	77.8	1¾	Butter	48.4*
2	Butter	66.4	2	Butter	68.0	2	Butter	47.7			

*Infection developed at close of period.

that on olive oil the percentage retention is sometimes 25 per cent or more better than butter (subject W. S—h, Table II; and subjects B—r and D—m, Table III), the difference being comparable to the average figures found with soy bean oil. However, in the two C—n infants, who were studied on both these fats, it is difficult to attribute the somewhat better retention of soy bean oil to age alone.

In order to throw further light on this question of the value of a second double bond, we made some comparisons between pure olein* and linolein.* Studies were made in three infants, the details of which are given in Table IV.

TABLE IV

FAT RETENTION OF PREMATURE INFANTS ON PURE OLEIN AND LINOLEIN

PERIOD		FAT FED	AGE (MO.)	WEIGHT (KG.)	LENGTH OF PERIOD (DAYS)	FAT INTAKE (GM./DAY)	FECAL FAT (GM./DAY)	FAT RETENTION	
								(GM./DAY)	% OF FAT INTAKE RETAINED
K—i	1	Linolein	¼	1.89	5	8.82	2.14	6.68	75.8
K—i	2	Olein	½	2.03	5	11.97	4.26	7.71	64.4
S—h	1	Linolein	¾	2.02	5	12.47	2.87	9.60	77.0
S—h	2*	Olein	1	2.19	5	13.38	4.17	9.21	68.8
S—h	4*	Linolein	1½	2.74	5	12.24	3.64	8.60	70.3
H—m	1†	Olein	½	2.16	6	9.26	3.38	5.88	63.5
H—m	3†	Linolein	1	2.33	5	13.59	6.77	6.82	50.2
Average—Olein periods			½	*2.13*	*5⅓*	*11.54*	*3.94*	*7.60*	*65.6*
Average—All linolein periods			*1*	*2.25*	*5*	*11.78*	*3.86*	*7.93*	*68.3*
Average—Linolein, excluding post-infectious periods			½	*1.96*	*5*	*10.65*	*2.51*	*8.14*	*76.4*

*Infection with digestive upset between period 2 and period 4.
†Infection with digestive upset between period 1 and period 3.

In none of these periods was the retention as high as in our previous studies on premature infants. This may have been due to the fact that the feeding contained monoglycerides and diglycerides or to the fact that the infants in this group were distinctly younger. We are inclined to accept the latter explanation, for we observed no untoward effect in normal infants when a similar preparation of olein was fed; in fact our best retention figures were obtained with this material.

The comparisons between the olein and linolein were not as conclusive as we had hoped. Unfortunately an infection developed in the premature ward during the course of this work. We continued our studies on two subjects when the infection and its effect on the digestion were apparently over, but in view of the chemical findings it may

*These were prepared synthetically from the pure fatty acids (95 per cent or more pure) and glycerin. The final products contained considerable monoglyceride and diglyceride although the larger part consisted of triglyceride.

be doubted whether either of these infants had completely returned to normal. We are, however, presenting the results *in toto* for what

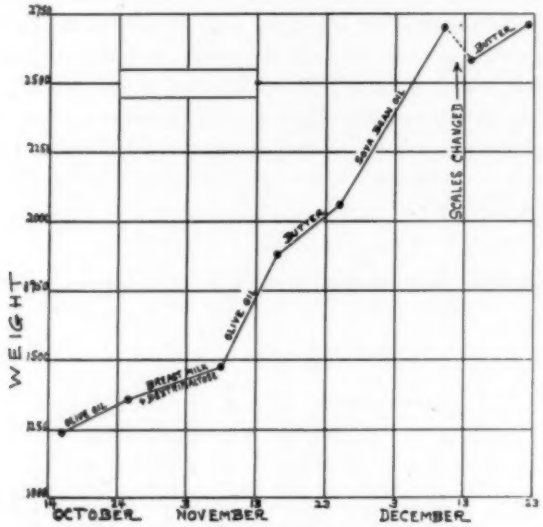

Chart 1.—C—n, Twin "A."

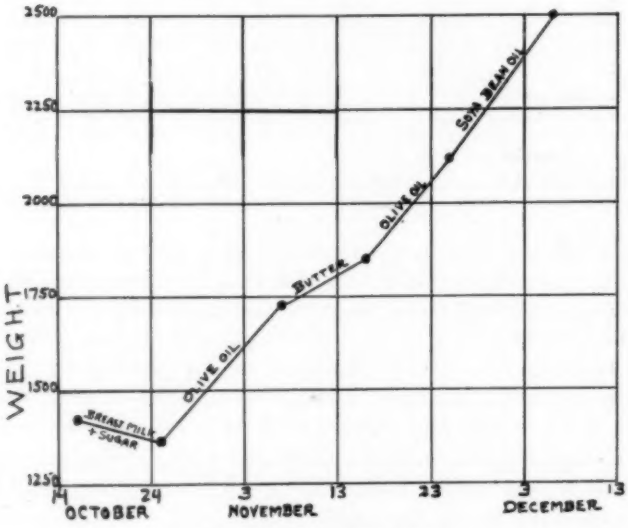

Chart 2.—C—n, Twin "B."

they are worth. If we exclude the postinfectious periods, we are left with a pair of unquestionably good periods on infants K—i and S—h in which the retention of linolein is distinctly better; the effect of age

should have favored the olein, for it was fed when the infants were a week older. Even if we include the postinfectious periods, the linolein still gives a slightly higher average retention figure.

The evidence obtained—either in the comparisons between olive and soy bean oil or in those between olein and linolein—is not conclusive, but it points in the same direction as that obtained by us in our study of normal infants, suggesting that an additional double bond possesses a slight advantage from the point of view of fat absorption.

As we have pointed out elsewhere[1] the weight curve may give fallacious information as to the value of a particular type of feeding, particularly when it is followed for only a short period of time; the retention of water and electrolytes alone may be responsible for gain

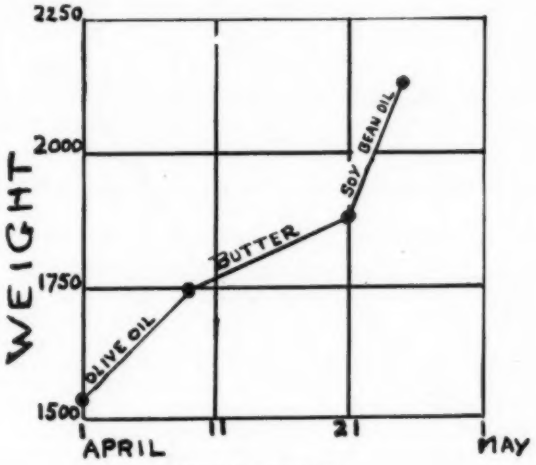

Chart 3.—Baby H—l.

in weight. Conversely, improvement in nutrition may not be immediately shown in the weight curve. However, if, as we have reason to believe, the substitution of more readily absorbable fats for butter serves to produce a significant improvement in nutrition, such an improvement might well be reflected in the weight curve. In some of our premature infants little or no change was observed in the weight curve, even though chemical determinations showed that more fat was being absorbed. But in more than half of our cases a striking upturn in the weight curve followed the substitution of olive oil or soy bean oil for butter. Such curves are shown in Charts 1, 2, 3, and 4, and appear to offer confirmatory evidence of the value of the more readily absorbable fats in the nutrition of these patients. Of particular interest are the observations on the identical C—n twins during the first weeks of life. One of these infants was started on a cow's milk

feeding in which olive oil was substituted for butter. This infant gained weight from the start, at no time falling below his birth weight, in contrast to his twin who was fed similar quantities of breast milk with added carbohydrate, in whom the usual postnatal loss of weight occurred.

It seemed of interest to ascertain whether the poor fat absorption of premature infants is associated with difficulty in splitting fat. It will be recalled that the full-term infants studied by us[1] were able to split fat completely, the so-called "neutral fat" fraction of their feces consisting in reality of unsaponifiable material. In order to obtain information upon this point, fat partitions were carried out in fourteen experimental periods on premature infants. In no instance was fat-splitting found to be complete, the true neutral fat of the feces being

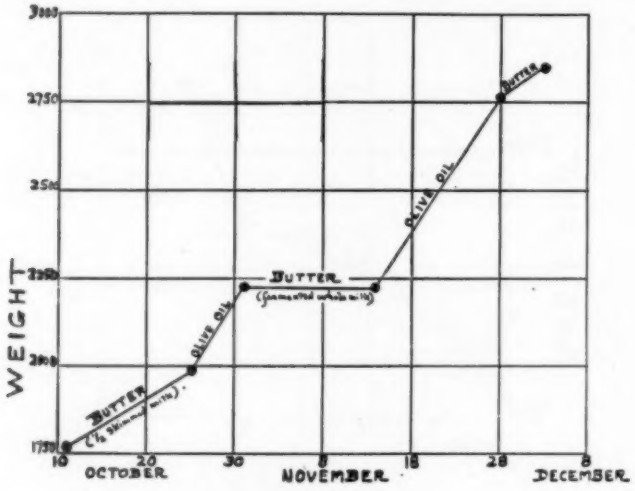

Chart 4.—Baby J—k.

found to exceed 0.2 gm. a day on diets of whole milk. The unsaponifiable matter was invariably in excess of that found in full-term infants, indicating that difficulty is experienced in the absorption of this fraction also. We are not prepared to say whether the difficulty in fat absorption in the premature infant is due to poor fat splitting, but at least it is of interest that both functions are impaired in these subjects.

The question may well be raised as to whether the results obtained with premature infants and twins are applicable to other groups of poor fat absorbers. We do not believe that any such generalization is justified; each group will have to be studied independently. A limited experience with infections and postinfectious states has given us the impression that considerably less benefit is to be expected here

from the substitution of olive oil or soy bean oil for butter than with premature infants; the unsaturated acids are by no means spared by the process which interferes with fat absorption. Whether a material gain can be accomplished by changing the fat in these circumstances we are not prepared to say. Ladd[3] reported a series of malnourished infants who gained weight more rapidly after the substitution of olive oil for butter fat; his conclusions as to the efficacy of homogenized olive oil were said to be confirmed by metabolism experiments which, however, were not published. Other writers[4] have felt that it was inadvisable to use olive oil in the presence of digestive upsets, a judgment which we believe to have been based on the appearance of the stools rather than that of the patient. Naturally, under conditions when much of the food fat appears in the stool, the stools will be more liquid when a liquid rather than a semisolid fat is fed.

CONCLUSIONS

1. We have confirmed observations in the literature that premature infants and twins have marked difficulty in fat absorption.

2. A very striking difference was found in the ease with which they absorb particular fats; olive oil and soy bean oil being far more completely absorbed than butter fat.

3. The improvement in nutrition when these fats are substituted for butter is often promptly reflected in the weight curve.

4. Some further evidence was obtained that the presence of more than one double bond in a fatty acid chain favors fat absorption.

5. Fat splitting is less complete in the premature infant than in the full-term infant; the retention of unsaponifiable material is also impaired.

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STUDIES IN INFANTILE ALLERGIC ECZEMA

II. Serum Lipids, With Special Reference to Saturation of the Fatty Acids

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IN CONTINUATION of a study of the serum lipids (cholesterol, phospholipids) in infantile allergic eczema, published in 1933,[1] we had just begun an investigation of the fatty acids when Hansen's[2] paper on this subject appeared. Wishing to obtain data for comparison with his, we modified our program in some respects and the results here presented cover practically the same ground as those of Hansen. The number of cases, both with and without eczema (normal controls), is, however, considerably larger than in his report.

It will be recalled that Hansen determined cholesterol, total fatty acid, iodine absorption, and the iodine number of the fatty acids in the serum; concluding that the serum cholesterol and fatty acids in eczema are slightly less than in normal controls and that the serum fatty acids are less unsaturated; hence, that the unsaturated fatty acids should be given consideration as an etiologic factor in the disease.

Methods.—Cholesterol was determined by the method of Myers and Wardell[3] on the dry residue left by evaporation of the alcohol-ether extract but without preliminary saponification, as Bloor[4] recommends. Hansen used Bloor's method. It is generally believed that the two show good agreement.

For fatty acids, the method of Bloor[4] was followed except that the alcohol-ether extract was kept at the boiling point for one minute instead of the "few seconds" recommended by Bloor, which appeared to be insufficient. Hansen also used Bloor's method.

Iodine numbers were determined by Yasuda's[5] method, based upon that of Rosenmund and Kuhnhenn but without preliminary saponification, an omission recommended by Page, Pasternak, and Burt[6] whose modification was followed by Hansen. It would appear that the results of the method used by Hansen and by ourselves are fairly comparable.

In one important respect our procedure differed from that of Hansen. Because of the fact that our patients were seen in the out-patient department we were unable, as Hansen was able, to obtain fasting samples. Most of our patients had been fed one to four hours before collection of the blood. Theoretically this constitutes a

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serious objection to our figures. Comparison, however, with those of Hansen shows that in the normal group our figures for total fatty acids are considerably lower on the average than those of Hansen; and in the eczema group, only slightly higher; also the iodine numbers in the normal groups in the two series show no significant differences. We are therefore inclined to believe that the time of bleeding in the two series plays a relatively small part in such quantitative differences as were observed. We have included a few older children in our series, but nearly all were within the same age limits as those of Hansen's series; that is, from five to eighteen months, and those outside these limits did not materially alter the averages.

In our series were sixteen normal individuals and fifteen with allergic eczema.

TABLE I

NO ECZEMA (16 CASES)—NORMAL CONTROLS

CHOLESTEROL	TOTAL FATTY ACIDS	TOTAL LIPIDS	IODINE NUMBER	AGE
172	338	510	124	6 mo.
211	324	535	124	11 mo.
169	181	350	117	3½ mo.
141	195	336	114	7 mo.
213	340	553	107	5 mo.
162	229	391	125	5 mo.
124	307	430	86	2 mo.
121	299	420	111	10½ mo.
346	328	674	130	7 yr.
129	331	460	100	5 mo.
199	322	521	117	8 yr.
143	252	395	117	3 yr.
122	297	418	108	13 mo.
159	371	530	121	23 mo.
142	291	433	152	7 mo.
207	274	481	131	10 mo.
Av. 161	290	451	117	

TABLE II

ECZEMA (15 CASES)

CHOLESTEROL	TOTAL FATTY ACIDS	TOTAL LIPIDS	IODINE NUMBER	AGE
222	391	613	105	5 mo.
141	379	520	102	3 mo.
134	315	449	120	5 mo.
136	333	468	97	6 mo.
163	381	544	107	8 yr.
162	473	634	111	11 mo.
198	339	537	101	15 mo.
136	265	401	104	24 mo.
142	289	430	112	11 mo.
220	436	657	87	7 mo.
169	295	464	135	3½ mo.
168	254	422	140	10½ mo.
213	405	618	102	16 mo.
173	358	532	102	4½ mo.
138	318	456	80	2½ mo.
Av. 168	351	516	107	

TABLE III

SUMMARY AND COMPARISON WITH HANSEN'S DATA

	NO. CASES		CHOLESTEROL		TOTAL FATTY ACIDS		TOTAL LIPIDS		IODINE NUMBER	
	OUR CASES	HANSEN'S CASES	OUR CASES	HANSEN'S CASES	OUR CASES	HANSEN'S CASES	OUR CASES	HANSEN'S CASES	OUR CASES	HANSEN'S CASES
Averages										
Normal	16	6	161	185	290	361	451	546	117	111
Eczema	15	7	168	147	351	342	516	488	107	84
Range										
Normal			121-346	142-232	181-340	292-411	336-674	434-643	86-152	100-136
Eczema			134-222	118-160	254-473	261-443	401-657	409-586	80-140	69-104

COMMENT

Cholesterol.—In a previous study[1] of a different series of infants with eczema we found a considerable proportion with hypercholesteremia. It is instructive to find that in the present subsequent series the cholesterol was uniformly within normal limits and the average was almost exactly that of the normal controls. Hansen's figures, by contrast, show a much lower figure for the normals and a higher one for the eczema cases than our own.

Total Fatty Acids.—Our average figures for the patients with eczema are not notably different from those of Hansen (351 and 342, respectively) but in the normals are considerably lower (290 as compared with 361), and this is also true of the total lipids. The contrast between the normal and the eczema group in our data is the reverse of that in Hansen's; ours showing a higher figure in the eczema group, and Hansen's a slightly lower one.

Total Lipids.—The same difference as in total fatty acids, between our figures and those of Hansen, is seen in total lipids (sum of cholesterol and fatty acid) but to a somewhat more marked degree; our eczema group being about 14 per cent higher than the controls, and Hansen's about 10 per cent lower.

Iodine Numbers.—For the control group our average (117) is not significantly different from Hansen's (111). In our eczema group the average (107) is about 9 per cent below that of the normals; while in Hansen's it (84) was about 24 per cent below his normal average. An arrangement of the individual data in our series in order of magnitude brings out a fairly striking tendency to lower figures in the eczema group, which is somewhat obscured in the average by the effect of two high figures. Our data, therefore, support Hansen's conclusion that in eczema the fatty acids of the serum show decreased unsaturation as compared with those in normal children; but, in a quantitative sense, the degree of saturation is much less, both absolutely and also relatively to the controls.

It may be added that Dr. Donald C. Marshall, in a considerable number of cases of active eczema admitted to the Children's Clinic of this institution, has been unable to detect any clinical benefit from the administration of unsaturated fat in the form of corn oil, an observation not in accord with Hansen's later report.[7]

CONCLUSIONS

1. An investigation of the serum lipids in thirty-one infants and young children, fifteen with infantile allergic eczema and sixteen without that disorder (normal controls) showed that the individuals with eczema had (a) a very slightly higher average cholesterol, (b) considerably higher average total fatty acids and (c) total lipids, and (d) a moderately lower average iodine number for the fatty acids.

2. Our results confirm those of Hansen in that the serum fatty acids of patients with eczema tend to be less unsaturated than those of normal individuals. The degree of unsaturation in our patients with eczema did not, however, depart so far from the normal as was the case in Hansen's series. Our own experimental data and clinical experience have not convinced us that the factor of fatty acid saturation is of primary etiologic significance in eczema. We are rather inclined to regard it as secondary or incidental.

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THE EFFECT OF FEVER THERAPY ON RHEUMATIC CARDITIS ASSOCIATED WITH CHOREA

With a Preliminary Report on Fever Therapy in Rheumatic Carditis Without Chorea

Lucy Porter Sutton, M.D., and Katharine G. Dodge, M.D.
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I. Fever Therapy in Chorea With Carditis

OVER two hundred attacks of chorea have been treated on the Children's Medical Service of Bellevue Hospital with fever induced by the intravenous injection of triple typhoid vaccine. In this series there were sixteen children with definite signs of active carditis at the time of treatment and in addition twenty-seven others with clinically inactive rheumatic heart disease. Of the twenty-seven with inactive heart disease, seventeen had mitral insufficiency; nine had mitral insufficiency and stenosis; and one had mitral insufficiency and stenosis and aortic insufficiency and stenosis.

Because it has been frequently suggested that the presence of advanced heart disease or the presence of active carditis is a contraindication to this form of therapy, the group with active carditis is now being reported in detail.

Our criteria for the diagnosis of active carditis were:

1. Fever
2. Tachycardia
3. Change in the quality of the heart sounds
4. Presystolic gallop sound
5. Development of new murmurs
6. Change in the quality of the murmurs present, especially the presence of a high-pitched, shrill, musical quality in the apical systolic murmur (sometimes described as "sea gull" quality)
7. Change in rhythm (heart-block, or loss of sinus arrhythmia)
8. Electrocardiographic changes, chiefly prolongation of the P-R and QRS intervals
9. The presence of subcutaneous rheumatic nodules

While every case did not present all of the above findings, each one presented two or more, and the diagnosis of activity was made by at least two observers. In a few cases the diagnosis was made only on going back over the records. In these cases frequent notes on the

From the Children's Medical Service, Bellevue Hospital, and the Department of Pediatrics, New York University.

The study of chorea has been made with the help of a grant from the Josiah Macy, Jr., Foundation.

heart were not always made, so that it has been sometimes difficult to determine exactly when the signs of carditis subsided. In the majority of cases, however, the diagnosis was made before the beginning of fever therapy; the patients were watched with especial care, and frequent notes on the heart signs were made.

Besides the cases which are being presented, there was one child who had signs of activity on admission to the hospital, but these had disappeared before the beginning of treatment, and seven children in whom the presence of activity was suspected but in whom it could not be diagnosed on any objective basis. We appreciate the fact that there are cases in which the signs of cardiac activity subside promptly after a short time at rest in bed, but on the other hand the tendency to chronicity of the rheumatic infection is well known. We have observed many individuals in whom signs of subacute carditis, i.e., tachycardia, gallop, low-grade fever, weight loss, etc., persist for months in a child in the hospital. We also realize that there must have been other children in this series with a subacute carditis who gave no clinical signs. In this group would fall those children who presented no signs of heart disease during their attacks of chorea but who, after varying intervals without further rheumatic attacks, have appeared in clinic with definite organic heart disease. This group will be presented in a later paper. The only case which came to autopsy demonstrates this point well; this was reported in detail in a previous paper.[1] During her two admissions to the hospital the child had never shown any signs of cardiac involvement. There was an inconstant short systolic murmur along the left sternal border, but there had never been an apical murmur, and there was no cardiac enlargement. At autopsy, besides a hemorrhagic lobular pneumonia, there was an acute verrucose mitral valvulitis and chronic rheumatic valvulitis at the base of the aortic valve.

While we have not yet demonstrated that the disappearance of the signs of activity was the direct result of the fever therapy, we feel that their disappearance in the majority of cases by the time of the end of treatment is striking. Certainly the children were not harmed by this form of therapy.

Case reports of the sixteen patients who had chorea and also carditis follow.

Case 1.—Y. A., eight years old, was admitted Oct. 21, 1932, and discharged Mar. 31, 1933. This child had been followed closely for two years as a tuberculosis contact case. She had had growing pains for six months previous to admission but no other rheumatic history. Two weeks before admission no cardiac murmurs were heard. She was admitted after one week of mild choreiform movements. At that time tachycardia and an apical systolic murmur were present; two days later a middiastolic murmur at the apex was heard; the following day she had an acute arthritis of one finger. Her temperature was normal. White blood cells numbered 8,750 with 77 per cent polymorphonuclear leucocytes. Electrocardiograms showed no

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significant changes. Treatment for the chorea was begun on the fifth day after admission; fever was induced six times in eight days. The day following the end of treatment, the systolic murmur was softer and the diastolic barely perceptible. Ten days later the heart was slow and regular, rate, 78 with sinus arrhythmia. The day after the completion of treatment an urticarial rash developed; this lasted for two or three days only. Six weeks later typical erythema marginatum, which persisted off and on throughout the rest of her stay, appeared, but no further signs of active carditis developed. On discharge five months after admission the heart was not enlarged clinically or by x-ray, but systolic and presystolic murmurs were present at the apex. She was not seen from the time of discharge until the following autumn, owing to lack of cooperation of the parents, but on return to clinic in December, 1933, seven months after discharge, she had gained 14 pounds and showed no evidence of rheumatic activity. Since then she has been followed regularly both in the tuberculosis clinic and in the chorea clinic, without further evidence of rheumatic infection until June, 1934, when she was readmitted to the hospital with indefinite signs of carditis.

CASE 2.—M. B., six years old, was admitted June 20, 1933, and was discharged July 7, 1933. She had no rheumatic history until three weeks before admission when she complained of pain in the ankles, tired easily, had a series of severe epistaxes, and bruised more easily than usual. One week before admission choreiform movements developed. On admission she had a temperature of 100.4° F., mild choreiform movements, many small purpuric spots on trunk and extremities, an enlarged heart with tachycardia, marked presystolic gallop, an apical systolic murmur transmitted to the axilla and base, and a loud, rough, low-pitched middiastolic murmur. Electrocardiogram showed right deviation of the electrical axis. White blood cells numbered 8,400 with 76 per cent polymorphonuclear leucocytes. Treatment for the chorea was begun on the fourth day after admission; fever therapy was given six times in eight days. The heart rate had slowed down somewhat before the beginning of treatment, but the gallop and diastolic murmur were still present. The day after the end of treatment the gallop had disappeared; rate was 80 per minute; sinus arrhythmia was present; murmurs were the same. Three days later the diastolic murmur had disappeared, but a third heart sound was heard. Ten days after the end of treatment the rate was 70; sinus arrhythmia was present; sounds were of good quality; there was a soft systolic murmur at the apex, slightly transmitted to the axilla, but no diastolic or third heart sound. One month later she had a tonsillectomy under ether anesthesia with no exacerbation of signs of carditis, and she was discharged to the country in good condition with a cardiac diagnosis of enlarged heart, mitral insufficiency, Class I. She remained in the convalescent home for three months and, having gained 6 pounds, returned to the clinic. Her general condition was good in the winter of 1933-34, and her weight gain satisfactory in spite of the bad home conditions under which she lives. Her present cardiac diagnosis is enlarged heart, mitral insufficiency, and (?) stenosis, Class I.

CASE 3.—M. A. B., aged seven years, was admitted May 1, 1933, and was discharged July 28, 1933. She had no previous history of rheumatic fever. She was admitted with a history of severe chorea of three months' duration and had been in bed, unable to walk for five weeks. On admission the child was emaciated, dehydrated, and totally incapacitated by an extremely severe pseudoparetic type of chorea. A nodule was present above the left patella. The heart rate was 130/140; there was a marked presystolic gallop, a widely transmitted apical systolic murmur with a high-pitched, shrill, musical quality, and a short presystolic murmur. There was no fever; white blood cells numbered 12,400 with 74 per cent polymorphonuclear leucocytes; the electrocardiogram showed no significant changes. Fever treat-

ment for her chorea was begun on the fourth day. She was given fever fourteen times in two courses, covering a total period of twenty-six days. By the fourth day after the beginning of treatment, the heart rate had come down to 104, and sinus arrhythmia had reappeared, but the gallop and high-pitched, shrill quality of the systolic murmur persisted. Three days later this murmur was much lower pitched and softer, and by the tenth day after the beginning of treatment the gallop had disappeared; the rate was 80; the shrill quality of the apical systolic murmur had entirely disappeared, and the nodule had also disappeared. One month later the gallop reappeared for ten days with a peridontal abscess and fever. Later tonsillectomy was performed without exacerbation of her cardiac signs. On discharge the x-ray pictures showed no cardiac enlargement; there was a soft systolic murmur at the apex, slightly transmitted toward the axilla and an inconstant third heart sound. She was discharged to a convalescent home where she remained for about two months. She was well on return, having gained 7 pounds, but shortly after her return she again developed chorea; this time with no evidence of carditis. She was readmitted and remained in the hospital for three months and was then sent to a convalescent home for two months more. On her first return visit to clinic, Apr. 11, 1934, her temperature was 100.6° F., and she had a gallop and tachycardia. She was sent home to bed, and about ten days later when choreiform movements began, she was admitted to the hospital. Fever therapy was again given with subsidence of the chorea and disappearance of the signs of possible carditis.

Case 4.—A. C., nine years old, was admitted May 2, 1933, and was discharged June 3, 1933. She had a history of polyarthritis at five and one-half years and of three previous attacks of chorea. Two and a half months before admission, in the clinic, tachycardia and a gallop were noted; she was sent home to bed with a request to return to clinic in two weeks, but she did not. Three weeks before admission she began to have joint pains, and one week later chorea developed. On admission it was found that she had lost 6 pounds since her previous visit to the clinic; she showed moderate choreiform movements, an enlarged heart with double mitral murmurs, tachycardia and a gallop. The temperature was 100.6° F.; white blood cells numbered 10,000 with 90 per cent polymorphonuclear leucocytes; the electrocardiogram showed no significant changes. Treatment was begun on the second day after admission; fever was induced eleven times in sixteen days. The gallop began to grow less marked eight days after the beginning of treatment and had entirely disappeared by the last day of treatment. She was discharged to convalescent home one month after admission with a cardiac diagnosis of enlarged heart, mitral insufficiency, and stenosis, Class IIa. Since that time she remained well, gaining 20 pounds in the past year, until a few weeks ago, when she was readmitted to the hospital with signs of active carditis but without chorea.

Case 5.—A. A. C., aged ten years, was admitted May 4, 1933, and was discharged July 28, 1933. She had had two previous attacks of polyarthritis. Two weeks before admission she had had pain in her legs, acute arthritis of the left knee, and fever of 103° F.; one week later chorea began. On admission she showed mild choreiform movements, erythema marginatum on arms and trunk, and enlarged heart with poor quality sounds, a rough systolic murmur at the apex, transmitted to the axilla, a rate of 130/140, with a marked gallop. A soft diastolic murmur was first heard two days after admission. Temperature was 101° F. on admission and remained elevated at 100° to 102° F., during the eight days preceding treatment. White blood cells numbered 6,500 with 70 per cent polymorphonuclear leucocytes; the electrocardiogram showed no significant changes. Acute arthritis of the right knee developed on the first day after admission. Beginning on the ninth day after admission she was given fever six times in six days. The heart rate became some-

what slower, and the quality of the heart sounds improved although the gallop persisted and was still heard three weeks after the end of treatment. There then followed sixteen days before another note on the heart was made, which said: "No gallop; rate is slow; sinus arrhythmia; systolic and diastolic murmurs are definite; the diastolic follows a fairly loud second sound; this is often confused with a true gallop." It is therefore possible that the gallop had disappeared earlier than a review of the chart would indicate. She was discharged to a convalescent home where she remained for one month. During the winter of 1933-34 she was well, with steady weight gain, but in July, 1934, she again showed signs of active infection, with joint pains, epistaxes, slight weight loss, and occasional low-grade fever.

CASE 6.—A. B. C., eleven years old, was admitted Apr. 27, 1933, discharged June 10, 1933; readmitted Aug. 9, 1933, and discharged Sept. 6, 1933. Three years previously she had had chorea and carditis following appendectomy. The April admission was for four days of chills, fever, pain in the chest, and "bloody urine." On admission temperature was 101° F.; she appeared acutely ill, had an acute pharyngitis, an enlarged heart with double mitral murmurs, a much accentuated P_2 and tachycardia. The first urine examination showed 75 mg. of albumin, rare hyalin casts, from 2 to 3 red blood cells and from 8 to 10 white blood cells per high power field. Subsequent examinations continued to show a faint trace of albumin although the microscopic examination rapidly became negative. She ran an irregular fever to 101° F. for a week following admission; her temperature was then normal for three days. At this time choreiform movements began to be noticed, and she again began to run fever of 100° to 102° F. Five days after the beginning of the chorea a gallop was heard, and the P_2 became even more accentuated. The chorea had progressed rapidly in severity until it was classed as "severe moderate." Electrocardiogram on May 2, 1933, five days after admission, showed a rate of 88; P-R interval of 0.2 seconds; QRS interval of 0.08 seconds with a prolonged S-T interval in Lead I. Ten days later the day of the beginning of treatment, the P-R interval was still 0.2 seconds; QRS interval was 0.06 seconds, low and slurred, and there was slight right deviation of the electrical axis. Fever treatment for chorea was begun on the seventh day after the first abnormal movements were noted, and four febrile reactions in six days were sufficient to cause almost complete subsidence of her chorea. By the third day after the beginning of the treatment the gallop had disappeared; the P_2 had become less loud, and the rate was 100; the following day an electrocardiogram showed no significant changes, the rate being 92 and the P-R interval 0.16 seconds. She was discharged to a seaside convalescent home, perhaps somewhat sooner than she should have been, and was sent home after only a short stay there. She was apparently comparatively well at home for five or six weeks when chorea began again, and after one week she was readmitted. On admission choreiform movements were very mild, she had tachycardia and a gallop with a very loud snapping P_2. Temperature was normal, as were the white blood count and differential blood count. Because of the mildness of her chorea, she was observed for fifteen days before being given fever treatment, during which time the tachycardia and gallop disappeared, and the quality of the heart sounds improved. She was then given fever six times in eight days, during which time there was no reappearance of clinical signs of carditis. Two weeks following the end of treatment, an aortic diastolic murmur was first heard, which persisted. Three weeks later, having gained 5 pounds since admission, she was discharged to convalescent home, with a cardiac diagnosis of enlarged heart, mitral insufficiency and stenosis, aortic insufficiency, Class IIa. She remained in the convalescent home for three months and returned in January, 1934, having gained thirteen pounds during her stay. She continued to gain weight and do fairly well throughout the winter on a regime of extra rest and limited activity, until about the first of May, when

she began losing weight, having some fever, dyspnea, and precordial pain; she was readmitted to the hospital. She went steadily downhill, developing acute pericarditis with effusion, congestive failure, and acute glomerular nephritis; she died three and one-half weeks after admission. Autopsy showed active and inactive mitral and aortic valvulitis, active tricuspid valvulitis, acute fibrinous pericarditis, chronic adhesive pericarditis, and acute diffuse glomerular nephritis.

CASE 7.—A. D., aged six years, was admitted June 29, 1932, and was discharged Aug. 1, 1932. She had no previous rheumatic history. Six weeks before admission choreiform twitching had followed chickenpox and became progressively worse, especially since measles four weeks before admission. For one week she had had joint pains. On the day of admission, examination of the heart was negative; the chorea was severe with generalized hypotonia. The following day she developed acute arthritis of the right ankle and right great toe; a blowing systolic murmur at the apex transmitted to the anterior axillary line and to the base was heard; there was a gallop and tachycardia and an accentuated P_2. Temperature was 101° F.; and white blood cell count was 9,050 with 89 per cent polymorphonuclear leucocytes. The electrocardiogram taken one week later showed no significant changes. Temperature remained elevated for three days and was then normal for four days before the beginning of treatment. During this time the cardiac signs improved somewhat; the rate became slower, but the gallop persisted. Fever was then induced seven times in seven days. Two days after the end of treatment there were no clinical signs of active carditis; rate was slow and regular; there was no gallop; there was a systolic murmur at the apex transmitted toward the axilla, and the P_2 was somewhat accentuated. The x-ray examination, however, showed no definite cardiac enlargement. She was discharged to the country in good condition one month after admission. She remained in convalescent home for two and one-half months and has been followed regularly in clinic for the two years since that time. Weight gain has been satisfactory, and there has been no evidence of active infection at any time. At present her heart is not enlarged, and no murmurs can be heard.

CASE 8.—H. D., ten years old, was admitted Feb. 8, 1932, and was discharged Oct. 22, 1932. She had had polyarthritis at the age of three years; heart disease had been discovered when she was five, and she had had a second attack of polyarthritis followed by acute pericarditis with effusion at the age of seven. She had been followed in the cardiac clinic without recurrence since that time. She was admitted with a history of pain in the right knee and ankle and fever, for two weeks. On admission her temperature was 101° F.; she was pale and listless but not acutely ill; her right ankle was tender and painful but not acutely inflamed; there was tachycardia and an apical systolic murmur transmitted to the axilla. Four days after admission an apical diastolic murmur which persisted was heard. White blood cells numbered 12,100 with 80 per cent polymorphonuclear leucocytes. Although the signs were not definite, she was thought to have active carditis. For the next seventeen weeks there was little change in her condition. Her joint symptoms subsided, and she gained weight, but her temperature remained elevated, for the most part between 100° and 101° F. with occasional rises to 102° associated with an acute pharyngitis. Her heart signs remained the same, and, although they were not clear-cut, she was thought to have continued rheumatic activity in her heart. She was given two blood transfusions for a marked anemia, but she remained pale and listless. During the eighteenth week of her stay in the hospital she had a sore throat and temperature of 101.3° F.; four days later she complained of pain in her shoulder, and the next day choreiform movements were first noticed. At this time there was tachycardia, and a gallop was noted. She was observed for five days, during which time the chorea became more marked; her temperature remained elevated from 100° to 101° F., and the tachycardia and gallop persisted.

Fever was then induced six times in seven days. The day following the second fever, the gallop was no longer heard, and the heart rate was 100. Following the end of treatment the rate was 80; rhythm was regular; and there was no gallop or other clinical signs of active carditis. Her temperature, which remained below 100° for eleven days following treatment, again became elevated for about ten days during another attack of acute pharyngitis. Four days after the subsidence of this attack and about one month after the end of fever treatment, the electrocardiogram showed first-stage heart-block. The only previous electrocardiogram which had been taken was one week earlier; this showed a P-R interval of 0.19 seconds. Electrocardiograms taken every three days continued to show a block for eight days although during this time there were no clinical signs of activity. For the next two months her temperature remained normal; she continued to gain weight; and her general condition was fairly good. She then had a secondary tonsillectomy followed by an elevated temperature for about a week. When this subsided, she was discharged and sent home. Since her discharge almost two years ago, she has been followed in the clinic and has been doing, on the whole, fairly well. In the spring of 1933 she had a mild flare-up with arthritis and fever without signs of active carditis; this attack subsided on rest in bed at home. She returned to school in the fall of 1933 and continued throughout the winter 1933-34 without evidence of active infection, but in July, 1934, again developed polyarthritis and was admitted to another hospital.

CASE 9.—C. G., nine years old, was admitted Jan. 19, 1934, and was discharged Feb. 27, 1934. She had no previous rheumatic history. Choreiform movements began two weeks before admission, following a two-week illness of fever and rash. On admission she had severe chorea with marked hypotonia; heart was not enlarged, and no murmurs were heard; the rate was 144, and a marked presystolic gallop was present. The following day a systolic murmur at the apex and left sternal border was heard. Treatment was begun on the fourth day after admission; fever was induced seven times in eight days. The day following the first treatment, the gallop was no longer heard, and the heart rate had fallen to 100/112. By the fifth day of treatment the rate was 88; sounds were of good quality; and the systolic murmur had become less loud. Ten days following the end of treatment, the murmur was no longer heard. She was discharged to convalescent home in good condition with no abnormal findings in the heart, although the x-ray examination showed questionable slight enlargement. She remained in the country for six weeks where her weight gain was good. In June of this year she again developed chorea, but without any signs of carditis, and was admitted to the hospital and treated. No murmurs were heard at any time during this admission, and the heart showed no enlargement.

CASE 10.—M. H., aged eight years, was admitted Dec. 28, 1932, and was discharged Mar. 29, 1933. Though she was the youngest child in a rheumatic family, she herself had no known previous history of rheumatic fever; however, a systolic murmur at the apex had been heard following scarlet fever seven months before admission. Choreiform movements began from three to four weeks before admission, and fever had been present for three or four days. On admission she showed mild chorea; her heart was not enlarged; there was a tachycardia of 130, a much accentuated P_2, and at the apex a low-pitched, rather rough and loud systolic murmur transmitted only slightly. Temperature was 101° F. and continued to be elevated for three days; white blood cells numbered 10,400 with 86 per cent polymorphonuclear leucocytes. The electrocardiogram showed no significant changes. Three days after admission a mitral diastolic murmur was heard. The diagnosis of activity was somewhat questioned, but the presence of fever and tachycardia, the quality of the heart sounds, and the development and subsequent disappearance of a diastolic

murmur made it seem likely. Treatment was begun on the ninth day after admission, fever being induced four times in five days. At the time of the beginning of treatment the tachycardia had subsided, but the diastolic murmur was still present. On the last day of treatment the diastolic murmur was no longer heard. She was given prolonged rest in bed following the treatment; she gained five pounds, and except for an infected finger, made an uneventful recovery. On discharge there was a short untransmitted apical systolic murmur and the x-ray examination showed no enlargement. She was sent to a convalescent home where she remained four months. She was not brought back to the clinic until November, 1933, five months after her return from the country, when both she and her sister had had mild "twitchings" for several weeks. Although her chorea was very mild and there was no evidence of active carditis, she was admitted to the hospital because of the impossibility of adequate care at home. Her chorea subsided without treatment, and she was sent home in five weeks. Since that time she has done only fairly well. Weight gain has been irregular; she has had two attacks of cervical adenitis and sore throat; on her last visit to clinic in June, 1934, she had one small area of erythema on her arm, and activity of her rheumatic infection was suspected. We have been unable to persuade her mother to bring her into the clinic since that time. Her cardiac diagnosis when last seen was enlarged heart, mitral insufficiency, Class I.

CASE 11.—T. J., two years and ten months old, was admitted June 13, 1933, and was discharged June 29, 1933; he was readmitted July 7, 1933, and discharged Aug. 1, 1933. He had no previous rheumatic history. Choreiform movements had been present for one week. On admission he showed moderate chorea, an enlarged heart with a high-pitched, shrill, musical systolic murmur, tachycardia of 130/140, and a presystolic gallop. An apical diastolic murmur was definitly heard the day following admission. Temperature was normal; white blood cell count was 12,500 with 72 per cent polymorphonuclear leucocytes. Treatment was begun on the ninth day after admission. Fever had been given six times in eight days when he developed chickenpox and had to be transferred to a contagious disease hospital. On discharge his heart rate was 104; the apical systolic murmur was still high pitched and shrill, but the gallop had become protodiastolic in time. He was readmitted from the contagious disease hospital eight days later, when he showed no evidence of active carditis. His heart was questionably enlarged clinically and definitely so by x-ray examination; the rate was slow, and there was sinus arrhythmia; there was a soft systolic murmur at the apex transmitted a short distance toward the axilla and along the left border of the sternum to the base, and a short diastolic murmur at the apex. On discharge three weeks after readmission the diastolic murmur was no longer heard. During the winter of 1933-34 he has improved remarkably, having shown no evidence of recurrence of the rheumatic fever. At present his heart is not enlarged, and no murmurs can be heard.

CASE 12.—L. K., aged eleven years, was admitted May 28, 1933, and was discharged June 18, 1933. He had no previous rheumatic history. Three weeks before admission he had his first attack of "hives," which had persisted to the time of admission. One week before admission choreiform movements had begun and had progressed rapidly, so that on admission he presented a severe pseudoparetic chorea. His heart showed no enlargement clinically; the rate was 120; there was no sinus arrhythmia; there was an accentuated P_2, and a loud apical systolic murmur with a high-pitched, shrill, musical quality transmitted to the axilla. Temperature was 102° F., and remained elevated for two days before treatment. White blood cells numbered 12,850 with 81 per cent polymorphonuclear leucocytes. Fever was induced nine times in eleven days. During the period of treatment the shrill quality of the systolic murmur became less marked although it did not entirely dis-

appear until one week after the end of treatment, when the rate was 100 and sinus arrhythmia had returned. Nine days following treatment, the parents insisted on taking the boy home against advice, and it has been impossible to persuade him to return to clinic since that time.

CASE 13.—I. K., six years old, was admitted June 28, 1933, and was discharged Aug. 6, 1933. She had had no history of rheumatic fever until one month before admission when she had polyarthritis, followed in three weeks by choreiform movements. On admission her temperature was 103.6° F.; there was an acute arthritis of the left wrist, severe choreiform movements with hypotonia, a questionable nodule on the scalp (which subsequently disappeared); her heart was not enlarged; the rate was 144/160; there was a slightly transmitted soft blowing systolic murmur and a questionable gallop. White blood cell count was 13,700 with 60 per cent polymorphonuclear leucocytes. Electrocardiogram showed only sinus tachycardia. Her temperature fell gradually to normal in six days; heart rate became slower, although still definitely accelerated, and the systolic murmur became much louder. Treatment was begun on the ninth day after admission. Fever was given six times in nine days with rapid marked improvement in her chorea. During the treatment a short diastolic murmur was heard for several days. By the end of treatment the heart rate was 112; sinus arrhythmia had reappeared, and the questionable gallop and the questionable nodule had disappeared. One week later the heart rate was 84 and remained down for the rest of her stay. On discharge the x-ray examination showed no cardiac enlargement, and there was only a soft untransmitted apical systolic murmur. She did beautifully for six months after discharge, gained weight well, and was entirely free from signs of rheumatic activity. She was therefore allowed to return to school in February, 1934. Four days later she developed severe polyarthritis and was readmitted to the hospital. On admission besides polyarthritis, she had a very severe carditis and later developed chorea. She remained in the hospital three and one-half months and was recently sent home to remain in bed, very much improved, although with signs of low-grade activity still present.

CASE 14.—A. L., nine years old, was admitted Dec. 14, 1932, and was discharged May 3, 1933. She had had severe chorea without signs of carditis six months before, but no other rheumatic history. Her present attack began two weeks before admission. On admission she had moderate choreiform movements and a temperature of 102.6° F., which remained elevated for the week preceding treatment. Active carditis was suspected because of tachycardia, an extremely labile pulse rate, and the recent appearance of a short diastolic murmur. Six days after admission the heart rate was 120; a definite gallop was heard; the electrocardiogram showed a P-R interval of 0.21 seconds, and the chorea had become severe. Treatment was begun on the ninth day, fever being induced twelve times in seventeen days. The fifth day after the beginning of treatment, the pulse was 80/90, and the gallop was no longer heard. From then on throughout the remainder of the treatment and of her stay in the hospital, the pulse rate remained down and no further evidence of carditis appeared. An electrocardiogram made after the second treatment showed a P-R interval of 0.18 seconds, and one taken one week later, a P-R interval of 0.14 seconds and sinus arrhythmia. On discharge following tonsillectomy three months later, the x-ray examination showed no cardiac enlargement; there was a soft, blowing, systolic murmur, maximum at the apex, and transmitted just to the left of the apex and to the base, and a short middiastolic murmur. Six weeks after discharge no diastolic murmur was heard. At this time, about five months after the clearing of her previous attack, she again developed chorea, this time of moderate severity, but without any evidence of active carditis. She was readmitted and given fever therapy.

Since her discharge in August, 1933, she has done well without any recurrence of chorea or carditis. Her cardiac diagnosis is enlarged heart, mitral insufficiency, Class I.

CASE 15.—M. R., ten years old, was admitted Nov. 14, 1930, and was discharged Dec. 23, 1930. She had had one previous attack of chorea at the age of six years, but no other rheumatic history. The present attack, following a head cold, began two days before admission. On admission she showed mild chorea, a heart slightly enlarged to the left, tachycardia and gallop, poor quality heart sounds, and a soft systolic murmur at the apex, transmitted to the axilla. By the first day of the treatment, the sixth day after admission, the rate was somewhat slower, but the gallop was still definitely present. Fever treatment was given seven times in seven days. The day following the last treatment, the heart rate was 88; rhythm was regular, no gallop was heard; and the systolic murmur had become fainter. For the remainder of her stay the rate remained down, and no further gallop was heard. A late soft diastolic murmur was heard at the apex from about one week after the end of treatment for ten days, but it was not heard during the last two weeks of her stay. The x-ray pictures showed cardiac enlargement with accentuation of the right auricular and left ventricular curves. She was discharged with a diagnosis of enlarged heart and mitral insufficiency. Since that time she has had two mild attacks of chorea, one in July, 1931, which was treated with fever therapy, and one in April, 1932, which subsided on rest in bed alone. For the past two years she has had no chorea or other evidence of rheumatic activity; her heart no longer shows enlargement either clinically or in x-ray pictures, and there is only a very faint systolic murmur best heard along the left sternal border. In October, 1933, she began to lose weight rapidly and to run an irregular afternoon fever. She was admitted to the hospital and when found to have tuberculosis (childhood type of primary lesion) she was transferred to a tuberculosis hospital.

CASE 16.—S. T., aged five years, was admitted Apr. 25, 1932, and was discharged June 3, 1932. He had no previous history of rheumatic infection. Choreiform movements had begun three weeks before admission, and one week after the onset he had pain for one day in his right knee and ankle. On admission he had moderate chorea with moderate hypotonia, a clinically enlarged heart, with a much accentuated P_2, a gallop, no tachycardia (pulse 80/90), a loud blowing apical systolic murmur with a high-pitched, shrill, musical quality, transmitted to the axilla and base, and a short, rough middiastolic murmur. His temperature was normal; white blood cells numbered 6,100 with 75 per cent polymorphonuclear leucocytes; the electrocardiogram showed right deviation of the electrical axis. Treatment was begun on the fifth day. He was given fever induced by intravenous triple typhoid vaccine for three days, and after an interval of three days fever was induced twice more by means of blanketing and hot water bottles alone. Since his second reaction to vaccine had been poor, on the third day tight blanketing was used in addition to the vaccine, with the result that accidentally his temperature reached 109.8° F. He was cooled off from this very high fever quite rapidly by exposure alone, but his temperature was above 104° F. for a total of about nine hours. Except for some vomiting, dehydration, and some acidosis, he seemed to suffer no ill effects from this extreme hyperpyrexia. Following the first two fever treatments, there had been no change in the heart signs, but the third day following the temperature of 109.8°, there was a striking change; the rate was 90; there was no gallop; the systolic murmur had lost its high-pitched, shrill, musical quality; and the diastolic murmur was no longer heard. From then on no further signs of active carditis developed, and tonsillectomy was performed three weeks after the end of treatment without exacerbation of activity in the heart. He was discharged with a diagnosis of enlarged heart and mitral insufficiency. During the two years since discharge he has had no chorea or other evidence of

TABLE

SUMMARY TABLE OF THE SIXTEEN CASES OF CHOREA WITH CARDITIS

CASE	ADMISSION CARDIAC DIAGNOSIS	SIGNS OF ACTIVE CARDITIS	NO. OF FEVER TREATMENTS	DAYS DURATION OF THERAPY	DURATION OF CLINICAL SIGNS OF CARDITIS
1	a. Rheum. b. Acute carditis c. S. T.* d. E. & F.	Tachycardia Development of systolic and diastolic murmurs under observation	6	8	End of therapy: rate slower, murmurs softer. 10 days after end of therapy: rate 78, S. A. present.
2	a. Rheum. b. E. H., M. I. Acute carditis c. S. T. d. I	Fever on admission Tachycardia Gallop Quality of systolic murmur Presence of diastolic	6	8	End of therapy: no gallop, rate 80, S. A. present. 4 days later: diastolic murmur no longer heard.
3	a. Rheum. b. Acute carditis c. S. T. d. E. & F.	Tachycardia Gallop Nodule High-pitched, shrill, apical systolic murmur	14	26	4 days after beginning of treatment: rate 80, S. A. present. 6 days later: no gallop, rate 80, no nodules. Systolic, soft and low pitched.
4	a. Rheum. b. E. H., M. I. & S. Acute carditis c. S. T. d. IIa	Fever on admission Tachycardia Gallop (present 2½ months before adm.)	10	15	End of therapy: no gallop, no tachycardia.
5	a. Rheum. b. E. H., M. I. Acute carditis c. S. T. d. IIa	Fever Tachycardia Gallop Poor quality heart sounds Development of diastolic	6	6	End of therapy: rate slower; gallop still present. 5 weeks after end of therapy: gallop gone.
6	a. Rheum. b. E. H., M. I. & S. Acute carditis c. S. T. d. IIa	Fever Tachycardia Gallop Much accentuated P_2 Prolonged P-R interval	4	6	End of therapy: no gallop, rate slow, P_2 less loud, P-R interval normal.
7	a. Rheum. b. Acute carditis c. N. S. R. d. F.	Fever Development of: Slight tachycardia Gallop Accentuated P_2 Systolic murmur	7	7	2 days after end of therapy: no gallop, rate slow.
8	a. Rheum. b. E. H., M. I. Acute carditis c. S. T. d. IIa	Fever Tachycardia Gallop A-V block (developed *after* treatment)	6	7	3 days after beginning of therapy: no gallop, rate 100. End of therapy: no gallop, rate 80.

*Diagnoses were made according to the criteria for the classification and diagnosis of heart disease of the Heart Committee of the New York Tuberculosis and Health Association. Abbreviations used are: E. H., enlarged heart; M. I., mitral insufficiency; M. S., mitral stenosis; A. I., aortic insufficiency; A. S., aortic stenosis; N. S. R., normal sinus rhythm; S. A., sinus arrhythmia; S. T., sinus tachycardia; E.,

I

TREATED BY ARTIFICIAL FEVER INDUCED BY TRIPLE TYPHOID VACCINE

COMMENT AND SUBSEQUENT COURSE IN HOSPITAL	COURSE SINCE DISCHARGE	DISCHARGE CARDIAC DIAGNOSIS	PRESENT CARDIAC DIAGNOSIS
6 weeks later: erythema marginatum which persisted throughout stay. No further signs of active carditis.	Well for 16 mo. when she developed indefinite signs of rheumatic activity.	a. Rheum. b. M. I. & S. c. N. S. R. d. IIa	a. Rheum. b. E. H., M. I. & S. c. N. S. R. d. IIa
T. & A. 1 mo. after therapy with no exacerbation of rheumatic activity or of carditis.	No evidence of rheumatic activity since discharge 11 mo. ago.	a. Rheum. b. E. H., M. I. c. N. S. R. d. I	a. Rheum. b. E. H., M. I. & S† c. N. S. R. d. I
Gallop reappeared for 10 days 1 month later with peridontal abscess and fever. T. & A. done with no recurrence of carditis.	2 attacks of chorea, the 2nd accompanied by indefinite signs of carditis, since discharge 1 yr. ago.	a. Rheum. b. ---- c. N. S. R. d. E. & F.	a. Rheum. b. ---- c. N. S. R. d. E. & F.
No reappearance of signs of carditis.	Well for 1 yr. In hospital at present time with signs of acute carditis.	a. Rheum. b. E. H., M. I. & S. c. N. S. R. d. IIa	a. Rheum. b. E. H., M. I. & S. Acute carditis c. S. T. d. IIa
Notes on chart poor. Signs may have subsided earlier. No other signs developed.	Questionable early signs of activity present, 11 mo. after discharge.	a. Rheum. b. E. H., M. I. & S. c. N. S. R. d. IIa	a. Rheum. b. E. H., M. I. & S. c. N. S. R. d. IIa
No further signs on this admission, but discharged too soon to the seashore.	Readmitted 2 mo. later with chorea and signs of carditis. Admitted to hospital 8 mo. later. Died 3 wk. later with pericarditis, congestive failure, acute nephritis.	a. Rheum. b. E. H., M. I. & S. c. N. S. R. d. IIa	Died
No further signs of carditis.	No rheumatic activity since discharge 2 yr. ago.	a. Rheum. b. ---- c. N. S. R. d. E. & F.	a. Rheum. b. ---- c. N. S. R. d. F.
1 mo. later Ekg. showed A-V block, which persisted for 8 days, but with no clinical signs of activity. Later T. & A. done with no exacerbation.	2 subsequent attacks of polyarthritis at yearly intervals.	a. Rheum. b. E. H., M. I. & S. c. N. S. R. d. IIa	a. Rheum. b. E. H., M. I. & S. c. N. S. R. d. IIa

possible heart disease; F., potential heart disease; I., functionally able to carry on normal activity; IIa, functionally able to carry on with slightly limited activity; IIb, functionally able to carry on with markedly diminished activity; III, signs of failure at rest in bed; T. & A., tonsillectomy and adenoidectomy.

TABLE I

CASE	ADMISSION CARDIAC DIAGNOSIS	SIGNS OF ACTIVE CARDITIS	NO. OF FEVER TREATMENTS	DAYS DURATION OF THERAPY	DURATION OF CLINICAL SIGNS OF CARDITIS
9	a. Rheum. b. Acute carditis c. S. T. d. E. & F.	Tachycardia Gallop Development of systolic murmur	7	8	After 1 fever: no gallop, rate 100. End of therapy: rate 88, murmur less loud. 10 days later: no murmur heard.
10	a. Rheum. b. Acute carditis c. S. T. d. E. & F.	Tachycardia Fever Accentuated P_2 Development of diastolic murmur	4	5	Rate slower at beginning of therapy. End of therapy: diastolic murmur no longer heard.
11	a. Rheum. b. E. H., M. I. Acute carditis c. S. T. d. I or IIa	Tachycardia Gallop High-pitched, shrill systolic murmur Development of diastolic murmur	6	8	End of therapy: no gallop, rate 104, systolic murmur still high pitched. 8 days later: soft systolic murmur, rate slow, S. A. present, short diastolic.
12	a. Rheum. b. Acute carditis c. S. T. d. E. & F.	Fever Tachycardia High-pitched, shrill systolic murmur No S. A.	9	11	During therapy systolic murmur became slightly softer. 1 week after end of therapy: systolic murmur soft and low pitched, rate 100, S. A.
13	a. Rheum. b. Acute carditis c. S. T. d. E. & F.	Fever Tachycardia Gallop? Nodule? No S. A. Development of diastolic murmur	6	9	End of therapy: rate 112, S. A. present, no gallop, no nodule, no diastolic murmur. 1 week later: rate 82.
14	a. Rheum. b. Acute carditis c. S. T. d. E. & F.	Fever Tachycardia Gallop Prolonged P-R interval Development of diastolic murmur	12	17	5 days after beginning of therapy: rate 80-90, no gallop. P-R interval normal before end of therapy.
15	a. Rheum. b. E. H., M. I. c. S. T. d. IIa	Tachycardia Gallop Poor quality heart sounds	7	7	End of therapy: rate 88, no gallop, sounds good quality, systolic murmur softer.
16	a. Rheum. b. E. H., M. I. Acute carditis c. N. S. R. d. I	Gallop High-pitched shrill systolic murmur Presence of diastolic	5	8	5 days after beginning of therapy: no gallop, systolic murmur soft and low pitched. No diastolic murmur heard.

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COMMENT AND SUBSEQUENT COURSE IN HOSPITAL	COURSE SINCE DISCHARGE	DISCHARGE CARDIAC DIAGNOSIS	PRESENT CARDIAC DIAGNOSIS
No further signs of carditis.	4 months later: chorea without carditis.	a. Rheum. b. X-ray E. H. c. N. S. R. d. E. & F.	a. Rheum. b. ---- c. N. S. R. d. F.
No further signs of carditis.	1 subsequent attack mild chorea without signs of carditis, since discharge 16 mo. ago.	a. Rheum. b. ---- c. N. S. R. d. E. & F.	a. Rheum. b. E. H., M. I. c. N. S. R. d. I
Diastolic no longer heard 3 wk. later.	No evidence of recurrence of rheumatism since discharge 1 yr. ago.	a. Rheum. b. E. H., M. I. c. N. S. R. d. I	a. Rheum. b. ---- c. N. S. R. d. F.
Taken home against advice 9 days after end of therapy. No signs of activity at that time.	Has not returned to clinic.	a. Rheum. b. ---- c. N. S. R. d. E. & F.	?
No further signs of carditis.	Did well for 6 mo. after discharge, then developed polyarthritis, severe carditis and chorea.	a. Rheum. b. ---- c. N. S. R. d. E. & F.	a. Rheum. b. E. H., M. I. & S. c. S. T. d. IIb
No further signs of carditis. Diastolic murmur gone 6 wk. after discharge.	1 subsequent attack of chorea, without carditis, since discharge 15 mo. ago.	a. Rheum. b. ---- c. N. S. R. d. E. & F.	a. Rheum. b. E. H., M. I. c. N. S. R. d. I
Soft, late diastolic murmur heard from 1 wk. after therapy, for about 10 days.	2 subsequent very mild attacks of chorea, without carditis, since discharge 3½ yr. ago.	a. Rheum. b. E. H., M. I. c. N. S. R. d. I	a. Rheum. b. ---- c. N. S. R. d. E. & F.
T. & A. 3 wk. after end of therapy with no exacerbation of carditis.	No further evidence of rheumatic activity since discharge 2 yr. ago.	a. Rheum. b. E. H., M. I. c. N. S. R. d. I	a. Rheum. b. ---- c. N. S. R. d. E. & F.

rheumatic activity. His general condition has been fairly good in spite of extremely low family income and bad hygienic care. At the time of this report his heart showed no enlargement, but there was a moderately loud systolic murmur at the apex transmitted slightly toward the axilla.

II. Fever Therapy in Rheumatic Carditis Without Chorea

Because of the conclusion, which was almost forced upon us, that these children seemed to have benefited by their fever therapy as far as their hearts were concerned, it seemed justifiable to investigate the effects of fever on various forms of rheumatic heart disease without chorea.

The most difficult type of child to handle therapeutically in the whole field of rheumatic infection is the child with evidence of subacute active rheumatic heart disease. As a rule, he is not acutely ill, but the activity of his infection, as evidenced by low-grade fever, progressive weight loss, tachycardia, gallop, skin manifestations, etc., may continue for months even under the best of surroundings and produce severe crippling of the child's heart. Up to the present time the only resources at our command for treating such a child have been elimination of foci of infection, prolonged rest in bed, high calorie and vitamin diet, and treatment of the usual anemia.

Since we felt that children with certain forms of heart disease would be too sick to stand the foreign protein shock, inevitably occurring with fever produced by intravenous vaccine, we had an apparatus built in which fever is produced by radiant energy from carbon filament bulbs, after the specifications of Dr. Stafford Warren, of Rochester University. This is a box which fits over a bed and in it a child's temperature may be raised to any desired level, slowly or quickly, and maintained for as long a time as is necessary or the condition of the child allows. The patients treated so far have been given a fever of approximately 106° F. for from two to five hours.

Up to the present time we have treated: (1) five children with subacute carditis, four of whom received two treatments each; (2) one girl, fifteen years old, with subacute bacterial endocarditis on the basis of long-standing rheumatic heart disease, with neither harmful nor beneficial results; (3) one child with very severe acute rheumatic carditis, accompanied by polyarthritis and chorea, to whom we gave two fever treatments. This child subsequently improved, but we were unable to say whether the fever therapy was a factor in the improvement.

We are presenting in detail the first two cases treated which are the only ones that have been observed long enough to enable us to draw even tentative conclusions.

Case 1.—I. B., seven and one-half years old, was admitted Nov. 21, 1933, and was discharged June 29, 1934. She had had polyarthritis at five and six years of age and is said to have had heart disease since the age of three years. The present illness began two weeks before admission with the development of an erythematous

rash. Three days later she began to feel tired and to have migratory joint pains and afternoon fever. On admission she appeared acutely and chronically ill, temperature was 101° F.; there was a widespread erythema marginatum; the heart was apparently enlarged; there were tachycardia, presystolic gallop, and accentuated P_2, a loud, harsh systolic murmur at the apex transmitted to the axilla and base, and a low-pitched, apical diastolic murmur. White blood cells numbered 10,200 with 72 per cent polymorphonuclear leucocytes.

For the next ten weeks her condition remained about the same. Except for one period of nine days, her temperature was above 100°, and sometimes 101° several times every week. In spite of complete rest in bed and extra nourishment, there was a progressive weight loss of 6 pounds. A widespread erythema marginatum was present most of the time. Tachycardia and gallop persisted. During the eighth week after admission rheumatic nodules were first noticed over both elbows and left external malleolus. The child continued to be listless and without appetite.

At the end of her eleventh week in the hospital she was given fever therapy by means of radiant energy for four hours, between 104° and 106.° During the treatment an extremely widespread erythema marginatum developed, which had disappeared by the next day. Following treatment her temperature remained consistently

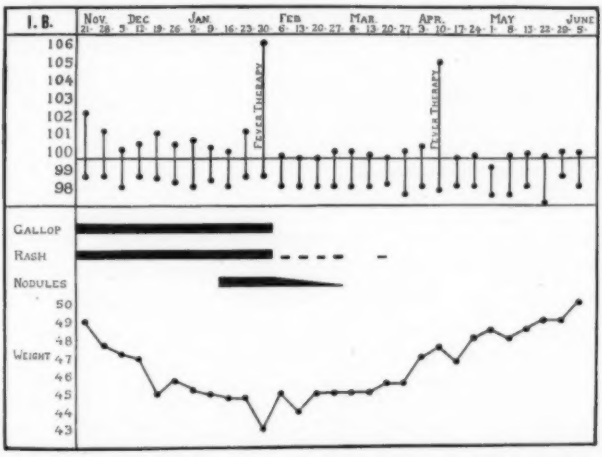

Chart 1.—(Case 1) Rheumatic carditis treated with fever produced by radiant energy. The temperatures indicated are the highest and lowest of a week.

below 100°. Her heart rate fell to normal, most strikingly shown in the drop in the sleeping pulse rate; her gallop disappeared; an occasional very small transient patch of erythema appeared, but no further widespread erythema marginatum; no new nodules developed and those present gradually grew smaller and were not detectable in the fourth week after treatment; she immediately began slowly to gain weight. More striking even was the change in the child's general appearance and attitude. Within a week after treatment she had changed from a listless, lackadaisical child with a poor appetite, to a lively active one, bright and interested in her surroundings, and with a ravenous appetite.

In the ninth week after treatment her temperature began to creep up above 100°, and her sleeping pulse rate began to be slightly elevated. Therefore, although her general condition continued to seem good and she was gaining weight, it was decided to give her another fever treatment in the hope of nipping in the bud a fresh exacerbation of her rheumatic infection. She was given four and one-half hours at 105° . During the height of the fever a few small patches of erythema marginatum

became evident, in no way comparable to that of the previous treatment. During the two and one-half months which she remained in the hospital following the second fever she continued to improve remarkably. Temperature and pulse remained normal; there was no further erythema of any sort; she continued to gain weight, more than regaining the six pounds she lost during the period before treatment. On discharge to a cardiac convalescent home no signs of activity could be detected; temperature and pulse were normal; white blood count and differential blood count and the erythrocyte sedimentation rate were normal.

CASE 2.—M. M., aged twelve years, was admitted Feb. 21, 1934, and was discharged May 29, 1934. She had had repeated attacks of chorea, almost annually, since the age of four and one-half years, but no other rheumatic history. We had followed her case since September, 1931, when she was treated with fever therapy for a moderate attack of chorea. Since that time she has had two very mild attacks of chorea, complicated by marked and definite habit spasms which were finally cured by psychotherapy. Her heart had never been enlarged, but there had been an apical

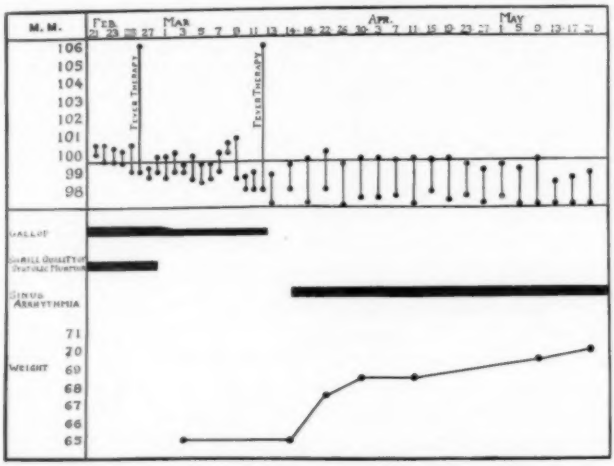

Chart 2.—(Case 2) Rheumatic carditis treated with fever produced by radiant energy. The temperatures indicated are the daily highest and lowest for the first two weeks, followed by the highest and lowest of four-day periods.

systolic murmur, transmitted slightly, present from the time of her first admission, and a diastolic murmur that had first been heard in December, 1932.

For two months previous to admission the mother had noticed tachycardia; dyspnea had developed when the child climbed one flight of stairs; and the child had been complaining of frequent precordial pain. Two weeks before admission she had had a sore throat and had been worse since that time. On admission her temperature was 100.4° F.; heart rate was 130/140; there was a marked presystolic gallop, an apical systolic murmur with a high-pitched, shrill, musical quality, and a short middiastolic murmur. No sinus arrhythmia was present. For the five days before treatment her temperature was above 100° every day, and the signs in her heart continued. In view of the observed tachycardia and precordial pain of two months' duration, she was thought to be a good candidate for fever treatment without further observation period in the hospital; on the sixth day she was given four hours of fever between 105° and 106° F. by means of radiant energy. Following this her temperature was still somewhat elevated, but in general at a lower level; the gallop persisted but was definitely less marked; her pulse rate, although still

somewhat elevated, was slower than before treatment; and the systolic murmur at the apex had lost its high-pitched, musical quality. Although she was improved, there were still definite signs of activity. She was therefore given a second fever treatment two weeks after the first, her temperature being kept at 106° for three hours. Following this the gallop was no longer heard; her temperature remained normal, and her heart rate, although occasionally elevated during the day, was consistently normal during sleep. The third day following treatment sinus arrhythmia was heard for the first time and persisted. Her general condition was much improved; she had an excellent appetite and gained weight steadily.

As she had a gonorrheal vaginitis, she could not be sent to a convalescent home. However, shortly following her discharge three months after admission, she was taken by her mother to the seashore where she was active and without complaints. At her first return visit to clinic she had gained another pound in weight and showed no signs of rheumatic activity.

SUMMARY

1. Sixteen cases are presented in which the diagnosis of active rheumatic carditis was justified. The patients were given artificial fever therapy produced by the intravenous injection of triple typhoid vaccine, for a concurrent chorea.

2. In nine of these patients all clinical signs of activity had subsided by the end of treatment. In the others signs were gone in from a week to ten days following the end of treatment.

3. Two cases are presented of subacute rheumatic carditis without chorea. The patients were given artificial fever therapy produced by radiant energy.

4. In one patient the signs of rheumatic activity cleared immediately following one treatment but recurred again to a much lesser degree eight weeks later. She was given a second fever treatment and has shown no clinical evidence of activity since.

5. The second patient improved following one treatment, but the signs of activity did not completely subside until after a second treatment two weeks after the first.

CONCLUSIONS

1. We believe that artificial fever therapy produced by the intravenous injection of triple typhoid vaccine or by radiant energy had no harmful effects on the course of the carditis in these children.

2. Furthermore, the application of the fever therapy seemed to have a beneficial influence on the course of the carditis.

3. The presence of a subacute carditis or of inactive rheumatic heart disease is not necessarily a contraindication to the use of fever therapy in the treating of chorea.

4. We suggest that the use of fever therapy in forms of rheumatic fever other than chorea deserves further study.

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VIRUS ENCEPHALITIS

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MOST of the cases of postvaccination encephalitis are reported from Europe. So recently has Newman[1] collected the reported cases here and abroad that repetition is not justified. The scant number of American cases finding their way into literature, seventy-four in all, justifies the following case report:

H. M. G., female, aged six years, was vaccinated by her family physician preparatory to going to school. Ten days later she became very drowsy, complained of headache, ran a temperature of 102° F., and later in the day had a convulsion which lasted one-half hour. When she recovered from the convulsion, she was stuporous and her temperature continued to rise. The following day she was admitted to St. Christopher's Hospital in convulsions with a temperature of 104° F. At that time her neck was slightly rigid, and her head was turned stiffly to the left. The eyes were open, and the pupils were dilated. They did not react to light. Ophthalmoscopic examination showed a marked venous tortuosity in both eyes. All of the extremities were spastic, and the reflexes were exaggerated, but at the time no Kernig, Babinski, or Oppenheim signs, or ankle clonus were present.

On the left arm there was a vaccination that was clean and healthy, typical of a ten- to twelve-day mark. No other physical findings of importance were noted. After this convulsion which was followed by several minor ones, she was in a state of coma which lasted for three days in all. Vomiting occurred frequently during the first four days in the hospital. The temperature remained between 103° and 104.3° F.

The cerebrospinal fluid pressure registered 20 mm., specimens having 50 to 55 cells, polymorphonuclears predominating. Sugar was present, and globulin was increased. The blood count showed a slight leucocytosis and the differential ratio was normal. During the comatose state fleeting positive Babinski signs and ankle clonus were noted.

On the sixth day of illness the child recovered consciousness and recognized her mother. The temperature started to come down and in five days was normal. From then on the convalescence was uninterrupted. No mental or nervous changes occurred. Two years later she was robust and mentally clear and alert. There were no behavior changes.

The vaccination ran a normal course never showing any unusual inflammation or infection. The scar can be completely covered with a ten-cent piece. The denudation method was employed. Incidentally, she had had no previous immunizing agent.

COMMENT

Postvaccination encephalitis is pathologically different from epidemic encephalitis. Flexner[2] calls attention to the difference in histopathology that can be summed up in the following:

From the Jefferson Medical College.

Postvaccination encephalitis shows adventitial and periadventitial round cell infiltrations distributed throughout the brain and cord. Myelin degeneration which gradually fades into normal myelin structure may be seen about smaller vessels. The characteristic softening or microglia proliferation about the blood vessels of the white substance of the central nervous system resembles the action of a toxic substance. Epidemic encephalitis is proliferative and infiltrative. The lesions are almost always confined to the brain and chiefly to the basal gray matter. Lymphocytes are found in layers in the perivascular lymph spaces. Postvaccination encephalitis is more widespread, is unevenly distributed, and is more partial to white matter.

Clinically, postvaccination encephalitis is marked by the triad of headache, vomiting, and pyrexia, at the onset, followed by rigidity of the neck, coma, and in many cases, convulsions. Temporary paralysis is insisted upon by English writers as an accompaniment. The course is stormy and alarming from the outset and the prognosis is grave. The vaccination shows no deviation from the usual picture of a "take," but it does not have to be a successful vaccination to be responsible for the syndrome under discussion. When not fatal, complete recovery mentally and physically takes place. This is very surprising in view of the above pathologic picture as presented by the fatal cases.

So much emphasis has been laid upon the differentiation between postvaccination encephalitis and epidemic encephalitis that but scant attention has been given to a comparison between postvaccination encephalitis and the encephalides following the acute exanthemas and a few other infections.

Encephalitis following measles has been reported by Musser and Hauser,[3] Ferraro and Scheffer,[4] and others. This encephalitis occurs during or shortly after the attack of measles. Clinically the signs and symptoms as described by these authors are identical with the picture of postvaccination encephalitis as portrayed above. With but very slight difference in the extent of cord involvement, the pathology is also similar in the two conditions. In fact the descriptions of Flexner's postvaccination encephalitis, and Musser and Hauser's, and Ferraro and Scheffer's postmeasles encephalitis are strikingly similar, and their published microscopic pictures emphasize the closeness of the relationship between these conditions, but none call attention to it.

Flexner's observation noted above assumes added significance therefore when he states that the lesion of postvaccination encephalitis is typical of the action of some toxic substance. Since virus has been recovered in the cerebrospinal fluid in the postvaccination encephalitis and not in the vaccinated who do not suffer with encephalitis, it might be fair to assume that the toxic substance is a virus. That there is a relationship between the virus of postvaccination encephalitis and the virus of postmeasles encephalitis is strongly upheld by Armstrong.[5]

Encephalitis is quoted as a complication of varicella and variola by practically all of the recent textbooks but no clinical picture is presented. Appended is a case that can with propriety be classed in this category:

Patient R. K., seven-year-old boy, developed fever, delirium, and vomiting ten days after the onset of varicella. He complained of headache. In forty-eight hours he became stuporous, then comatose with convulsive tremors. This persisted for three more days after which he recovered consciousness. He had had measles, mumps, and pertussis. He has never been protected against diphtheria nor vaccinated.

This case came under the observation of Dr. M. M. Bekir in the third day of the encephalitis, who called me to see the child on the fourth day at Memorial Hospital, Roxboro. At that time physically the patient presented these salient findings. The eyegrounds showed some venous engorgement. He had a rigid neck, a positive Kernig sign, an exaggeration of all reflexes, and a positive Babinski sign. There were convulsive movements of all extremities, athetoid in type. A temperature of 103° F. persisted for one week. The spinal and cisternal tap showed a clear fluid under pressure, averaging from sixty to eighty cells, with polymorphonuclear cells predominating. Sugar was reduced, globulin increased. His blood counts showed a secondary anemia and the white blood count averaged sixteen thousand with 87 per cent polymorphonuclears, 12 per cent small mononuclears, and 1 per cent eosinophiles.

He made an uneventful recovery, and his mental faculties seem unimpaired. However, but one year has elapsed since his illness.

Note the similarity between this case and the case of postvaccination encephalitis and the tendency to some meningeal irritation as it obtrudes itself upon the pictures.

Since both of these children reported recovered, demonstration of their pathologic lesions is impossible. It is at least evident that virus infections can, and do, produce encephalitis that differs from the type of encephalitis known as "epidemic encephalitis" or "encephalitis lethargica." There is also a close bond between virus-produced encephalides despite the marked difference in the clinical pictures of vaccination, smallpox, measles, chickenpox, and scarlet fever.

It is presumed as before stated that vaccine virus is the etiologic factor in postvaccination encephalitis because the virus has been recovered from the cerebrospinal fluid. This would lead to the presumption that similar viruses operate to produce the similar clinicopathologic pictures in the other encephalides that sometimes accompany the exanthemas. Indeed it might even argue for the virus etiology of scarlet fever. However, this is not complete proof.

It might also be assumed that a usually innocuous virus is rendered virulent by any one of the viruses causing any one of the exanthemas. Gorter,[6] of Leyden, supports this view. He agrees with Bok of his own country that the virus encephalides are all one and the same disease due to the activation of the ordinarily innocuous virus. He states that in the Netherlands they have rarely recovered vaccine virus from the cere-

brospinal fluid in postvaccination encephalitis. The German authorities, however, assert that they have recovered it in a high percentage of cases. This is possibly a technical discrepancy.

Pleomorphic streptococci, protozoa, and yeasts are assumed to be activated by virus. The almost omnipresence of streptococci in health or disease has certainly given it the distinction of causing a multitude of diseases of which it is probably primarily innocent. The actual etiologic factor is still open to argumentation for final scientific solution.

Despite the lack of definite information concerning etiology, it is presumed to offer preventive measures against postvaccination encephalitis, but the other virus encephalides are still evasive. Empirical as they are, a few prophylactic rules may be productive of successful results. These rules are based on sound clinical observation. Clinical observation, after all, needs no apology made for it.

First, the rarity of postvaccination encephalitis following vaccination in infants under one year of age cannot be explained away by the statement that fewer children are vaccinated at that age than at a later period in life. That infants are not apt to be sensitive to virus in these early months of life is generally accepted. The same holds true of secondary vaccinations at any age. Couple this with the advantage of more careful attention to wounds in infants as compared with the dangers of contamination and dirt in the preschool age group, and there is a potent argument for early vaccination.

Second, if the infant has been further desensitized to virus by other immunizing agents, notably diphtheria toxoid, it has even less chance of developing encephalitis. This must be noted, however, that vaccination performed too soon after the toxoid injection will probably not be successful. Particularly is this true of alum precipitated toxoid. Allow *at least* a month to elapse after diphtheria immunization before vaccinating.

Third, the single slight one-eighth-inch scratch or puncture method should be the procedure employed in performing the vaccination. Only healthy children should be vaccinated. The multiple scratch, multiple puncture, or denudation method allow relatively large quantities of virus access to the patient, whereas the recommended procedure allows but little. Particularly is this true if the virus is rubbed into the scratch only until the edges of the scratch become ischemic and the residue of vaccine wiped off completely with sterile cotton. It has been shown that while virus multiplies in the human, this small amount takes sufficient time to catch up to the larger amounts and desensitizes individuals before it reaches the maximum of the large dose administered.

The probable relationship of the encephalides enumerated in this discussion demands the closest scrutiny. Their tendency to occur in the

lymphatic types and the more robust subjects may complicate the study, but it does point to virus implication since the virus multiplies in these subjects more rapidly than in their opposites.

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345 SOUTH NINETEENTH STREET

SOY BEAN (VEGETABLE) MILK IN INFANT FEEDING

Results of Three and One-Half Years' Study on the Growth and Development of 205 Infants

Fred Rittinger, M.B. (Tor.), Leon H. Dembo, M.D.,
and Gilberta G. Torrey
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IN December, 1932,[1] we published a preliminary report on the results obtained with fifty infants who were fed soy bean milk for a period of six months or longer.

Up to that time we had been using a flour made from the Mammoth Yellow beans, to which were added malt syrup, lactose, cottonseed oil, calcium and magnesium lactate, the chlorides of sodium and potassium, and the glycerophosphates of iron and calcium, butter fat, and cod liver oil. These additions were made because of certain deficiencies in the bean itself, notably mineral salts and carbohydrate. A study of the vitamin potency of the flour indicated that the quantities of vitamins A, D, and B complex in the mixture were adequate for the normal growth of rats.

The composition of the flour, plus the above additions, was as follows:

	Percentage
Moisture	2.50
Protein	23.69
Fat	20.20
Carbohydrate	48.31
Total ash	5.30
Starch	0.50
pH	5.50 (reliquefied)

One ounce of this powder equaled 125 calories. Reliquefied, in the proportions of 35 gm. of the powder to 8 ounces (236 c.c.) of boiled water, gave the following formula:

	Percentage
Protein	3.60
Fat	3.07
Carbohydrate	7.30

(One ounce equals approximately 19.4 calories.)

The infants were studied in two groups: (1) breast-fed babies receiving an insufficient quantity, and (2) babies fed exclusively on soy bean milk.

An analysis of the composite and individual weight charts at that time indicated that the majority of the infants did well, making good average gains and developing normally.

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Since publication of this preliminary report we have made several changes in the composition of the original soy bean formula. The chief changes were made in the protein-carbohydrate ratio since it was thought that the protein percentage in the original formula was proportionately high. The final formula, designated as soy bean E, and which we have used for the past two years, has the following composition:

	Percentage
Protein	14.00
Lactose	53.00
Fats (cottonseed, butter, etc.)	17.80
Ash	5.00
Moisture	2.50
Iron (as metal)	0.0142
Calcium	0.80
Phosphorus	0.50

Reliquefied, in the proportions of 35 gm. of the powder made to 8 ounces with water, the formula gives: protein, 2.12 per cent; fat, 2.71 per cent; carbohydrate, 8.00 per cent; with a caloric equivalent of 19.6 to the ounce. This gives approximately a 4:1 ratio of carbohydrate to protein.

Over two hundred infants were observed while receiving this "milk" and their respective weights and development noted. An analysis of the results in feeding this preparation demonstrates its superiority over the original formula. (Charts 1 and 2).

SOY BEAN AND SKIMMED MILK

There are several varieties of the soy bean (Mammoth Yellow, Manchu, Illini, etc.) which differ in their relative proportions of the amino acids, notably tryptophane, lysine, etc. It was thought, therefore, that the bean flour in combination with skimmed milk might yield improved growth factors because of the vegetable-animal protein combination, plus a fortified amino acid constituency. Accordingly, we prepared two formulas known as SW and SSW, the S and SS signifying the skimmed milk protein added, the W indicating a wheat germ addition for the vitamin B complex.

	Soy Bean SW (Percentage)	Soy Bean SSW (Percentage)
Protein (soy bean)	11.00	7.00
Protein (skimmed milk)	3.00	7.00
Lactose	53.00	53.00
Fats	17.80	17.80
Ash	5.00	5.00
Moisture	2.50	2.50
Iron (as metal)	0.1042	0.0142
Calcium	0.50	0.50
Phosphorus	0.17	0.13

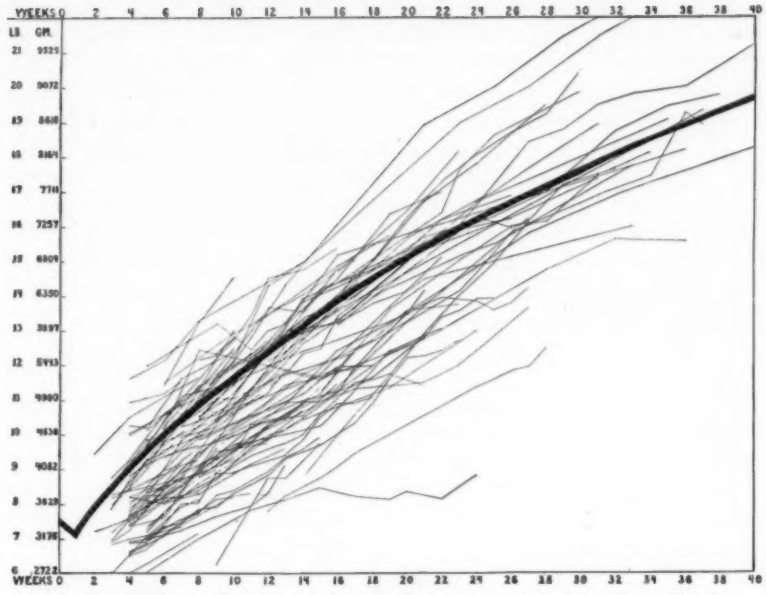

Chart 1.—Eighty-four infants on breast feeding plus soy bean milk E plain.

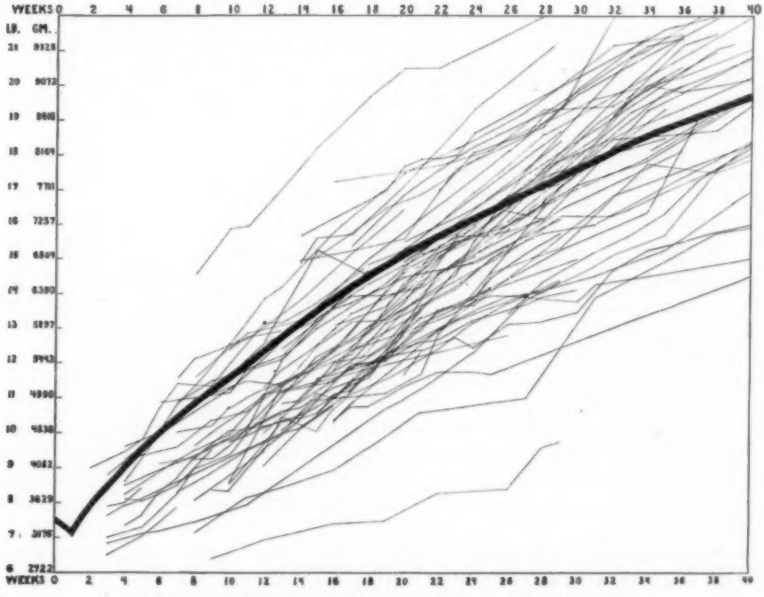

Chart 2.—Sixty-nine infants on soy bean milk plain only.

From these formulas it will be seen that the chief difference lies in the protein percentages of the added skimmed milk. Charts 3 and 4 show the weight curves of fifty-two infants fed on the soy bean-skimmed milk preparations, twenty-seven of whom received additional breast milk. While there is no apparent, marked difference as compared with the babies fed on the plain soy bean preparation, we felt, nevertheless, that the combined proteins afforded a definitely reinforced, prophylactic soy bean food. Tso[2] has demonstrated that it requires a higher protein caloric intake of the soy bean to equal the nutritive properties of a cow's milk protein-caloric intake in lower proportion. It would seem, therefore, that a combination of the two types of protein offers a distinct advantage from the standpoint of nutrition and growth.

VITAMIN POTENCY

A complete vitamin assay was included in our preliminary report, which showed that the preparation contained an adequate amount of the A, B and D complexes. The introduction of wheat germ in the new formulas was made for the purpose of increasing the B complex. Vitamin D potency is further fortified by including cod liver oil in the soy bean flour mixture.

METABOLISM STUDIES

Nitrogen.—During the past few years investigators have reported careful studies on the nitrogen metabolism of infants fed on soy bean protein.[3, 4, 5, 6] In these investigations different soy bean preparations were used, varying from the ground whole bean to water-soluble fractions of the bean as the source of protein. In addition, various percentages of soy bean protein were fed with a view to determining the ability of the infant to utilize the vegetable protein.

Our investigations were undertaken in order to determine the retention of nitrogen by the infants fed on our soy bean preparations, namely, soy bean E (plain), SW, and SSW.

The infants, seven in number, were selected from those coming regularly to the dispensary and had been fed exclusively on one of the soy bean preparations for some time prior to admission to the hospital. They were placed on a canvas bed strapped at the four corners to the upright supports of the crib and strapped to the canvas, the buttocks resting on a padded rim of an aperture cut in the canvas support. A stool pan was held in place beneath the buttocks and a special tube was attached to the infant for the collection of urine.

A sample of food sufficient for the entire experiment was thoroughly mixed and daily portions weighed from this sample. In this way it was possible to determine accurately how much nitrogen, calcium, and phosphorus were provided in the quantity given to the baby. Any portion of the food refused was measured and proper allowance made.

The infants were kept on the metabolism bed for a total of four days, during which twenty-four-hour collections of the urine and feces were made. The samples were thoroughly mixed and portions for analysis taken. Nitrogen was determined by the Kjeldahl sulphuric acid method with copper sulphate as the catalyst.

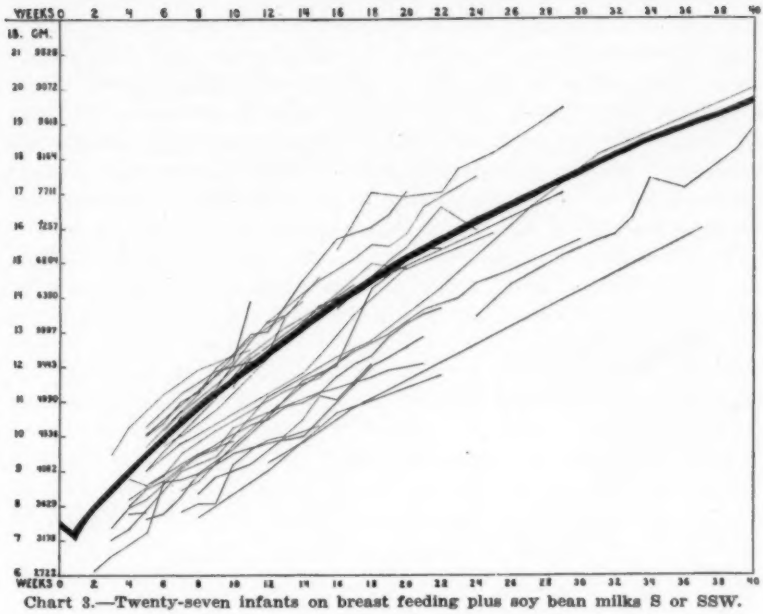

Chart 3.—Twenty-seven infants on breast feeding plus soy bean milks S or SSW.

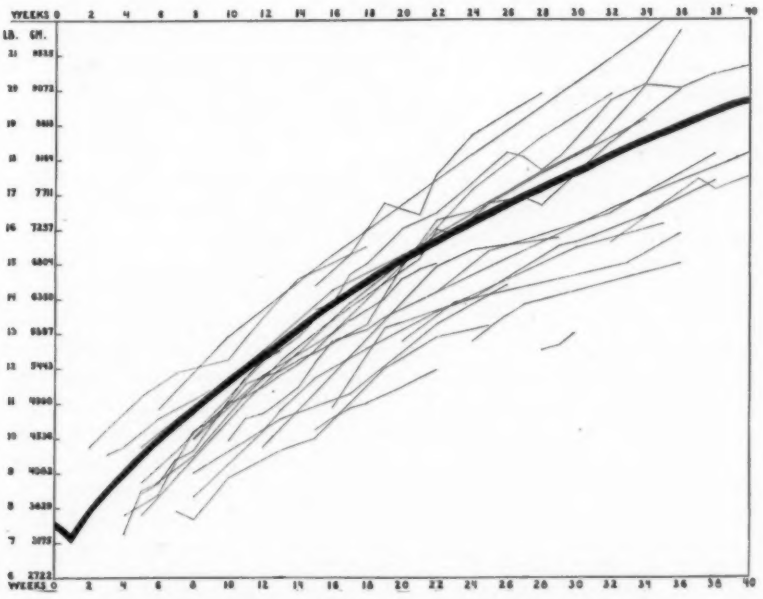

Chart 4.—Twenty-five infants fed soy bean milks S and SSW.

The infants varied in weight from 2,800 to 7,650 gm. They were fed the particular soy bean preparation under investigation, the protein calories varying from 11.8 per cent to 15.8 per cent. Exact analysis of each sample fed to the individual infant showed slight variations in the composition. Infant C——r was fed each of the three different formulas (E, SW, SSW) so that exact comparison with the same system and conditions is possible. All the infants were offered liberal feedings, depending on appetite and tolerance, and were fed at four-hour intervals. The caloric intake varied from 70 to 217 per kilogram.

The fresh weight of the stools varied somewhat but averaged 470 gm. for the period of the investigation. This is somewhat higher than the figure reported by Tso and Chu,[5] whose average for the same period was 215 gm. This might be accounted for by the fact that our preparations were made from the whole bean while Tso used only a portion of it. The stools are usually very soft and moist. One analysis showed less than 20 per cent solids.

The nitrogen intake was higher in the case of Baby McN——l and lower in the case of Baby M——a, who ate less food and was a rather poorly nourished infant of a neuropathic constitution (Table I).

TABLE I

INFANT	BODY WT. IN GM.	CALORIES PER KG.	PROTEIN CAL. (PERCENTAGE)	NITROGEN INTAKE IN GM.	RETENTION OF N GM.	GM./KG.	UTILIZATION PERCENTAGE	RETENTION PERCENTAGE
H—i	7,650	70.0	15.8	3.525	0.665	0.085	80.5	14.4
McN—l	4,200	200.0	15.8	4.353	1.800	0.428	81.6	41.0
B—k (1)	2,800	217.0	15.8	3.880	2.648	0.946	---	69.1
B—k (2)	3,175	146.0	15.8	2.955	1.550	0.490	70.0	52.0
C—n E	3,940	108.0	13.0	2.320	0.757	0.192	78.5	32.2
J—e (SW)	3,770	112.0	14.5	2.391	0.895	0.237	66.0	37.4
C—r (SSW)	4,890	140.0	13.7	3.510	1.340	0.274	83.4	38.2
C—r (SW)	5,200	117.0	14.0	3.218	1.080	0.208	83.6	38.9
C—r (W)	5,250	114.0	11.8	2.755	0.624	0.120	70.0	23.0
M—a (SSW)	5,740	70.0	13.7	2.106	0.827	0.144	78.5	39.3

The utilization varied from 66 to 83 per cent, which compares favorably with other reports. The *retention* varied from 14.4 to 69.1 per cent. The very high retention in the case of Baby B——k (1) can probably be explained on the basis that the intake of nitrogen was very high during the period of study. This baby was premature, and therefore does not give a true index of the retention on this particular soy bean preparation. In general it can safely be stated from the results of this study that at a protein-caloric intake of approximately 13 per cent, the percentage of nitrogen retention is at a level approximating that of similar cow's milk feeding. Summarizing, then, the results of these metabolic investigations, we find:

1. At a protein-caloric level ranging from 11.8 to 15.8 the level of nitrogen retention was fairly high, varying from 14.4 to 69.0 per cent.

2. An arbitrary level for protein calories in the diet has been established at approximately 14.0 per cent.

3. Either plain soy bean milk or soy bean milk combined with skimmed cow's milk gives adequate retention of nitrogen when fed to infants.

Calcium and Phosphorus.—The calcium and phosphorus utilization was observed for five of the metabolism periods during which nitrogen balance was determined, the infants receiving the diet for considerable periods before being placed on the metabolism bed. Calcium was determined by the Shohl-Pedley method, and phosphorus by the colorimetric method of Benedict and Tice. Table II shows the results of these investigations.

TABLE II*

INFANT	CALCIUM				PHOSPHORUS				Ca:P RATIO
	INTAKE GM.	RETENTION GM.	GM./KG.	PERCENTAGE	INTAKE GM.	RETENTION GM.	GM./KG.	PERCENTAGE	
J—e (SW)	0.638	0.378	0.100	60	0.132	0.049	0.013	37	7.5:1
C—r (SSW)	0.812	0.272	0.058	33	0.270	0.151	0.031	56	2.0:1
C—r (SW)	0.702	0.363	0.070	51	0.238	0.155	0.030	63	2.3:1
C—r (W)	0.916	0.384	0.074	42	0.222	0.130	0.025	60	3.0:1
M—a (SSW)	0.496	0.214	0.037	43	0.166	0.092	0.017	53	2.2:1

*The authors wish to acknowledge the assistance of Miss Carla Zorn who performed the necessary analyses for the calcium and phosphorus studies.

The results in Tables I and II show a very satisfactory retention of all three elements; nitrogen, calcium and phosphorus. This is especially of interest in view of the diversity of the amounts of each element fed. The only exceptions are the phosphorus values for Babies J——e and M——a whose intakes were also very low. In all cases the phosphorus figure falls considerably below the amount that should be retained in order to fulfill the requirements given by Stearns.[7] About the same results were found by Tso, Yee and Chen,[8] and by Stearns[6] in their experiments with soy bean milk feeding.

Shohl and others[5] have indicated that the ratio of calcium to phosphorus should be approximately 6:4 for proper growth of bone and to supply phosphorus for tissue development. The above figures for retentions showing 2:1 and 3:1 ratios would therefore be much too high in calcium. This deficiency does not show up in the values for serum calcium and phosphorus given elsewhere in this paper, a result which corresponds to the findings of these authors: namely, that the body composition remains normal and the lack of phosphorus results only in retarded growth.

BLOOD STUDIES

Blood counts were made on a number of the infants; the average red cell count was 4,920,000, while the hemoglobin gave a good average of 13.9 gm. per 100 c.c. (Newcomer.)

Calcium and phosphorus levels of the blood serum were determined in twenty-nine infants using the Benedict and Booher modification of Clark's method. Infants had been on the soy bean food for a period of six months or more when the determinations were made. The average total serum calcium was 11.5 mg. per 100 c.c. The average serum phosphorus was 5.5 mg., both figures being within the normal range. Baby S. W., fed on the plain soy bean preparation in addition to breast milk, had a low level of calcium and phosphorus. However, there were no clinical signs of rickets, nor did a roentgenogram show positive evidence. Baby J. Y. was fed only on the plain soy bean milk, and, while the serum phosphorus was within the normal level, the serum calcium was under the normal range. Clinically this baby was negative as regards rickets; x-ray pictures were also negative.

The question of the *antirachitic value* of soy bean meal is discussed by Bischoff.[9] He compares soy bean meal (after the removal of most of the fat) with other cereals usually employed for the nutrition of infants and children, and mentions the importance of phosphoric acid derived from the abundance of lecithin present in the soy bean. The work of other investigators, who found that chestnut meal plus 10 per cent of soy bean meal maintained rats without rickets, is also discussed. Rachitic animals were given 1, 2, 10, 14, and 16 per cent soy bean without any sign of healing. Only at a diet content of 50 per cent soy meal was there satisfactory recovery as shown by roentgenograms. They believe that soy meal can be considered a valuable prophylactic, but that by ordinary methods too dilute a mixture and therefore not enough soy meal is actually supplied to the patient.

THE STOOLS

The stools, grossly, were of a greenish to slate-gray color, somewhat larger than those of cow's milk preparations. The number varied from one or two to five daily. There was no foul odor, and the consistency was normal. In our previous report the flora showed a predominance of gram-positive organisms, thus resembling that of the stools of normal breast-fed infants. It was thought that the addition of varying quantities of skimmed cow's milk to the soy bean flour might result in a different picture, namely, a swing to the gram-negative side. Accordingly, a complete analysis of stools taken from infants fed on the three formulas (E, SW, and SSW) was made by Dr. E. E. Ecker, of the department of pathology, Western Reserve University, all but one of which showed a high percentage of gram-positive organisms (Table III). His report follows:

"All the stools appeared normal and of normal consistency except Nos. 2 and 7. All the stools showed a dark green color. Nos. 2 and 7 were yellow green. No pathologic organisms of the colon typhoid group were observed following plating of the specimens on Endo agar. The greenish color of the stools was due to traces

of bile pigments since the stools gave a positive Gmelin test. Ether extraction showed some greenish coloration. No fat or free starch were found. Pea-sized pieces of each of the nine stools were emulsified in 2 c.c. of sterile physiologic salt solution. The emulsions, to which a few glass beads were added, were then vigorously shaken by means of a Wright eccentric hand centrifuge, and two standard loopfuls of each emulsion were smeared on each of the two slides. The slides were air dried, fixed by heat, and stained by the Jensen-Gram method. A total of 500 organisms covering several fields of both slides were counted."

From the results (Table III) it is clearly evident that with the exception of stool 5 the stools were composed of a high percentage of gram-positive organisms. Stools 2, 3, 4, and 6 gave a fairly high percentage of probable *B. bifidus-acidophilus* forms.

TABLE III

STOOL NO.	GRAM-NEGATIVE ORGANISMS (PERCENTAGE)	GRAM-POSITIVE ORGANISMS (PERCENTAGE)	COCCI ALL FORMS (PERCENTAGE)	GRAM-POSITIVE RODS (PERCENTAGE)	SLENDER AND SLIGHTLY CURVED GRAM-POSITIVE RODS B. BIFIDUS-ACIDOPHILUS (PERCENTAGE)
1	+ 20	+ 80	+ 10	+ 70	+ 6
2	18	82	+ 16	+ 66	+ 23
3	+ 5	+ 95	+ 34	+ 61	+ 18
4	+ 13	+ 87	+ 24	+ 63	+ 24
5	+ 64	+ 36	+ 8	+ 28	+ 4
6	+ 6	+ 94	+ 10	+ 84	+ 29
7	+ 28	+ 72	+ 43	+ 29	+ 9
8	+ 17	+ 83	+ 22	+ 61	+ 5
9	+ 20	+ 80	+ 7	+ 73	+ 3

ROENTGENOLOGIC STUDY

X-ray studies of the long bones were made of eighteen infants. These were checked for bone development and bone texture by Dr. Francis of the Brush Foundation. The results are shown in Table IV. The great majority of these showed good bony development and good texture, with no signs of rickets. In a few instances the pictures revealed suspicious evidence of rachitic changes, yet the serum calcium and phosphorus were well within the normal limits, and clinical signs were lacking.

DIGESTIBILITY AND BUFFER ACTION

That the protein of soy bean milk compares favorably with that of cow's milk from the standpoint of digestibility has been demonstrated by Adolph and Wang.[10] These investigators conducted a series of tests in vitro, the results showing that peptic digestion was greater for the soy bean milk than for cow's milk. This they attribute to the possibility of different linkages or to the fact that no hard curd is formed by acid. The optimal pH was identical for both at 1.66. The percentage of digestion was 57.6 for soy bean milk and 37.8 for cow's milk.

Experiments with trypsin revealed a greater digestibility, at the optimum pH, for cow's milk. Tryptic digestion was 61 per cent for soy bean milk at a pH of 10.2, while for cow's milk the percentage of digestion was 78 at a pH of 11.3. Experiments in vivo (rats) on a ten-day test showed the digestion of the soy bean milk to be about 84.9 per cent, while for cow's milk the average was 86.6.

Reid[11] conducted some experiments on a soy bean milk-egg preparation. He removed the husks from soaked beans, which were ground and filtered through cloth. This was boiled for fifteen minutes. Fifty grams of cane sugar, plus 30 gm. of egg yolk, 1 gm. of sodium chloride, and 2.5 gm. of calcium lactate were then added to each liter and the entire

TABLE IV

INFANT	AGE IN MO.	ROENTGENOGRAM		
D. H.	10	B.D.,* 9 mo.	B.T.,† fair.	No rickets.
S. W.	9	B.D., 9 mo.	B.T., light.	No rickets.
A. G.	9	B.D., 5 mo.	B.T., light.	Rickets suspected.
G. R.	8	B.D., 5 mo.	B.T., good.	No rickets.
J. B.	6	B.D., 3 mo.	B.T., poor.	Rickets suspected.
R. P.	12	B.D., 10 mo.	B.T., light.	No rickets.
D. N.	11	B.D., 5 mo.	B.T., good.	No rickets.
R. E.	10	B.D., 3 mo.	B.T., good.	No rickets.
R. B.	8	B.D., 5 mo.	B.T., good.	No rickets.
S. H.	8	B.D., 9 mo.	B.T., fair.	No rickets.
E. Q.	8	B.D., 3 mo.	B.T., light.	Rickets suspected.
E.M.	10	B.D., 9 mo.	B.T., good.	No rickets.
J. H.	8	B.D., 3 mo.	B.T., good.	No rickets.
C. M.	12	B.D., 18 mo.	B.T., light scars.	No rickets.
J. Z.	12	B.D., 5 mo.	B.T., fair.	No rickets.
G. M.	7	B.D., 2 mo.	B.T., good.	No rickets.
F. R.	10	B.D., 5 mo.	B.T., fair.	No rickets.
D. H.	11	B.D., 3 mo.	B.T., good.	No rickets.

*B.D., bone development.
†B.T., bone texture.

mixture spray-dried at 50 to 55° C. Peptic digestion in vitro showed boiled cow's milk and boiled, reconstituted soy egg milk equally digestible. At an acidity over 0.13 per cent of HCl, raw cow's milk was more digestible. Raw cow's milk was 25 per cent less digestible than the boiled, while raw soy egg milk was 50 per cent less. Tryptic digestion showed that boiled cow's milk digestion is much higher than either the raw cow's milk or soy-egg milk.

Chart 5 illustrates the buffer curves for the three preparations of soy bean milk (SW, SSW, and E). The acidity was determined by the quinhydrone electrode. It will be seen that the curves for the SW and E parallel each other closely up to the point where 20 c.c. of 0.2 N HCl was used. There is a greater divergence of the curve for the SSW preparation.

SOY BEAN MILK AND INFANTILE ECZEMA

In a previous communication[12] we reported on the results obtained in a small series of cases of infantile eczema, using the soy bean milk (E) as a dietary method of therapy. The rationale was based on the substitution of a vegetable protein for the animal protein of cow's milk, on the premise that the skin manifestations were due to sensitization to animal protein. This theory, and the subsequent use of soy bean milk as a dietetic "cure," was first suggested by Hill and Stuart.[13] Our results were, for the most part, good. However, it has been our experience that in a few instances, in spite of the fact that the causal factor points to a milk sensitization, we have been unable to clear the eczematous lesions by the substitution of soy bean milk.

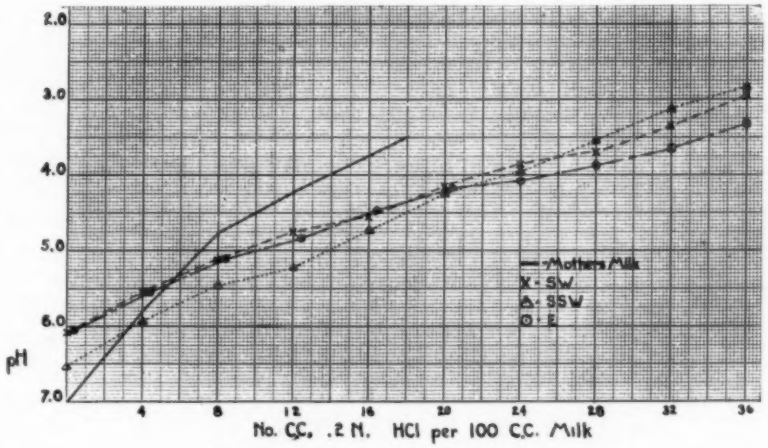

Chart 5.—Buffer curves for various milks.

Recent investigations by other workers have brought to light some interesting data on the question of the etiology of infantile eczema. It further suggests a possible explanation for the beneficial results obtained with soy bean feeding other than that based on the protein.

Shortly after our paper was submitted for publication[12] there appeared in the literature a very interesting series of reports by Hansen,[14] and Hansen and Burr[15] on the possible explanation of the etiology of infantile eczema. Burr and Burr[16] found that rats underwent marked skin changes when suffering from unsaturated fatty acid deficiency disease. This suggested that some dermatologic disorders of childhood, such as eczema, might be dependent on this dietary deficiency.

Hansen determined the iodine absorption number in ten cases of infantile eczema and in sixteen normal infants. This was followed by the determination of the total fatty acids, cholesterol, total iodine absorp-

tion of the serum, and the iodine number of the serum fatty acids in five normal and six eczematous infants. In the eczematous infants the average I.A.N. (iodine absorption number) was 383, while the controls averaged 539. He found that the iodine number of the serum fatty acids was abnormally low in infantile eczema during the active phase of the disease. Twenty-one determinations on eleven cases of eczema showed the average iodine number to be 82, as against 114 for the controls.

On the basis of these findings, he treated a series of cases of eczema by the administration of oils rich in unsaturated fatty acids. The diet and local treatment were the same for all. Out of a group of four infants, one was used as a control, the remaining three infants receiving supplements of linseed or corn oil. The iodine number of the serum fatty acids was subnormal in all four cases before treatment but increased to normal levels with marked improvement in the skin condition. The control infant, receiving no oil, failed to show definite clinical improvement, and the iodine number did not rise.

Further studies on the iodine absorption of serum in rats fed on fat-free diets revealed a low index, the highest iodine absorption of the "fat-free" animals being lower than the lowest I.A.N. of the control rats. The cholesterol and total fatty acids of the serum were also much lower in the rats on the fat-free diet.

It is obvious that further work along these lines must be done before we can draw conclusions as to its importance and significance in the matter of etiology. However, these investigators deserve a vote of thanks from pediatrists for what promises to lead us into an effective line of therapy.

The importance of their investigations from the standpoint of soy bean milk feeding lies in the relatively high proportion of the unsaturated fatty acids in soy bean oil. On the basis of their findings the question arises as to what factors are operative in the clearing of eczematous lesions by means of soy bean milk feeding. Are the beneficial results due to the substitution of the vegetable protein or to the unsaturated fatty acids in the soy bean oil?

The work of Hansen and Burr thus opens a new line of investigation, namely, the therapeutic effects of the administration of soy bean oil as compared with linseed and corn oil. It is our intention to apply this form of therapy to a series of cases of infantile eczema with the hope of being able to contribute some informative data.

CLINICAL RESULTS

The earliest age at which soy bean milk was started was two weeks. All infants were given supplementary doses (daily) of cod liver oil, averaging from 1 to 2 teaspoonfuls. Orange juice was, of course, included.

One group was started on food supplements (cereals and vegetable pulp) at three months, while the remaining groups were started at six months.

Chart 1 is a composite picture of the weight curves in a series of eighty-four infants fed on the plain soy bean milk with variable quantities of breast milk. As will be noted, the curves parallel the Holt line for the most part. A few show sharp breaks with a tendency to flattening. Several curves are broken by plateaus. Many of these occurred as a result of intercurrent infections. In a few instances we were

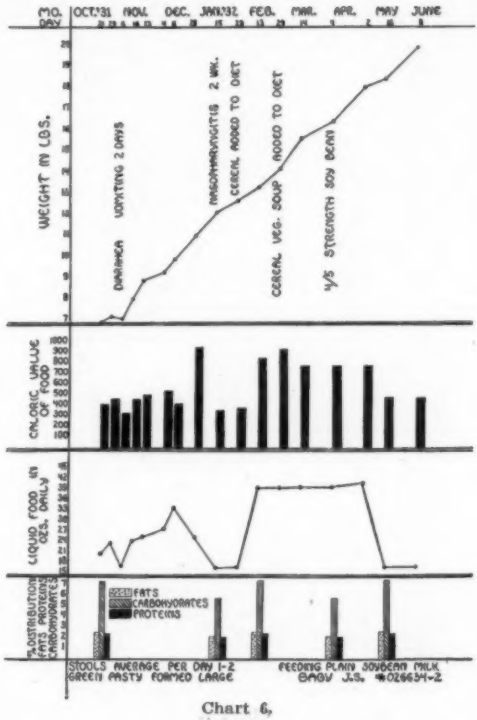

Chart 6.

unable to account for the poor gains. However, the composite curve compares favorably with similar curves from infants fed on cow's milk preparations.

Chart 6 is a representative, individual picture of progressive gains over a period of seven months on the plain soy bean milk feeding. It is interesting to note that in spite of a two-week period of parenteral infection there was no break in the upward trend of the weight curve.

Chart 2 shows the composite curves of a group of sixty-nine infants fed on soy bean milk only. There was no skimmed milk added, and they received no breast milk. These curves are, we believe, on a par

with the group mentioned above, who were given breast milk also. A larger number of the curves is above the Holt line, and the great majority closely parallel the line.

Chart 3 shows the curves of twenty-seven infants fed on breast milk plus the soy bean-skimmed milk mixture. Chart 4 represents a group of twenty-five infants fed on the soy bean-skimmed milk preparation minus breast milk. The curves in both of these charts further demonstrate the adequacy of the food.

Charts 7 and 8 illustrate the progress in two infants fed on the soy bean-skimmed milk mixtures. Baby N. D. (No. 031217) received a

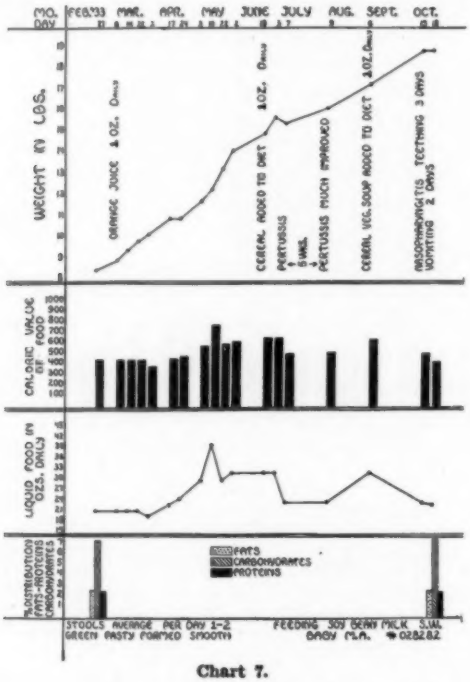

Chart 7.

higher percentage of skimmed milk protein than did Baby M. A. (No. 028282); yet there is little difference in their respective curves.

Growth and resistance to infections were good in practically all of the babies. The tissue turgor was excellent; their color was good; and their general development paralleled that of breast-fed infants and those fed on cow's milk preparations.

EFFECTS OF SOY BEAN MILK ON CONSTIPATION OF INFANTS

In our preliminary report we mentioned that a characteristic feature of the stools was the large bulk. This we attributed to the cellulose

roughage of the bean. During the course of our feeding experiments, we found that a complaint of constipation was a rarity. Because of this, and on the basis of the large fecal residues, we combined the soy bean flour with cow's milk feeding in a number of cases in which constipation had been a major complaint. Variable quantities were added to the cow's milk formulas, depending upon the requirements of the individual case. We found that the stool residues became greater in bulk and that there were from one to two good stools daily. We mention this as a suggestion for a mechanical type of laxative in cases in which constipation is troublesome. In the absence of conclusive facts

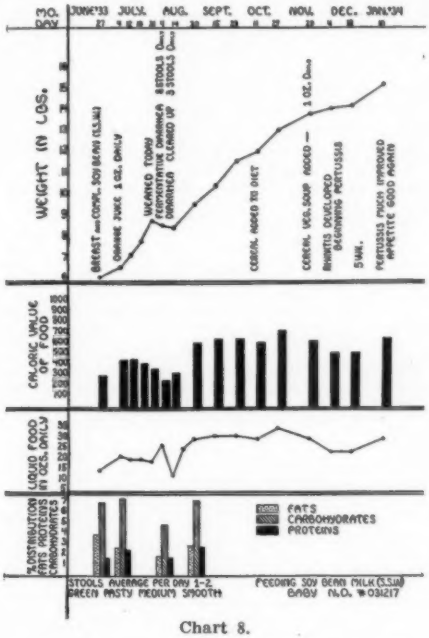

Chart 8.

as to the action of the soy bean flour in producing these large stools, we favor the theory of "roughage" action.

SUMMARY

1. A study of the results of soy bean milk feeding is presented, covering a period of three and one-half years. Two hundred five infants were fed this "milk" over variable periods. Growth and development, weight gains and their general progress point to the adequacy of this milk as a prophylactic food.

2. The preparations used have been shown to contain adequate amounts of the essential vitamins, and metabolic investigations have demonstrated a relatively high biologic value.

3. Soy bean milk in combination with various percentages of skimmed milk protein affords a food of high nutritional availability.

4. Blood studies have shown a normal range of calcium and phosphorus (serum), and roentgenologic studies demonstrate good bony development and texture with few exceptions. Suspicious signs of rickets in a few instances have not been corroborated clinically nor serologically.

5. The stool flora show a high percentage of gram-positive organisms, thus resembling those of breast-fed infants.

6. Soy bean milk is of practical value in the dietetic treatment of infantile eczema and in the treatment of constipation in infants by virtue of the "roughage" factor.

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RANGE AND STANDARD DEVIATIONS OF CERTAIN PHYSICAL MEASUREMENTS IN HEALTHY CHILDREN

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ACCURATE anthropometric standards are necessary for the study of growth changes, development, nutrition, and ductless glands. This requires quantitative measurements and statistical treatment of data.

For the most part, measurements of a large number of children have included only heights and weights.[1, 2] Transverse body diameters determine body build and are gradually assuming much importance in the study of children.[3, 4] Body build is here used in the strict sense of type of bony framework designating large-boned and small-boned individuals. State of nutrition has nothing to do with this definition of body build.

The necessity of an accurate, objective method of measuring body build is emphasized by the demonstration of definite relationships of body build to nutrition,[5, 6] to oxygen consumption,[7] and to physiology of the gastrointestinal tract.[8] There is a presumptive relationship between body build and mental and personality make-up.[9, 10, 11, 12, 13, 14] Finally, there are certain suggestive findings in the field of immunology which associate disease susceptibility with general massiveness or lack of it.[15, 16, 17]

Physical constitution is beginning to be recognized in America as a valuable approach in the appraisal of the child.[18] Galton[19] was a pioneer in the field of anthropometry and in the application of exact numerical values substituted for vague clinical estimates. He advocated recording measurements of body proportions, strength, keenness of sense, energy, intellectual capacities, and mental character. Anthropometry may become the best key to whether development is normal or otherwise. Endocrinologists consider divergence from certain physical standards as being due to endocrine dyscrasias.[20]

The need for tables of normal measurements is obvious. The authors have been doing anthropometric measurements on San Francisco children for the past five years and have collected 5,749 cases with ages ranging from six months to fifteen years.

Tables of constants presented are made up of measurements done on middle class, American-born, white children. They represent public school, private office practice, and hospital clinic populations. All

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children in the endocrine clinics and those suffering from any serious or chronic illness were excluded. We made sixty-three body measurements and worked out twenty-seven indices on the first one thousand children.

A number of these indices yielded substantially the same information and so were eliminated. Certain of the body measurements were found to contribute nothing toward classification of body build in the sense of designating large-boned and small-boned individuals, and consequently were not continued in the body build studies. Finally, thirteen measurements were chosen, and six indices were worked out from these as contributing differential items.

Technics of measuring were those described by Martin,[21] Hrdlicka,[22] and Draper[23] or those adopted by the International Anthropometric Agreement. Standard anthropometric instruments were used throughout. The large and small sliding calipers, spreading calipers, and anthropometric rod came from Zurich. Millimeter tapes with spring handles to regulate the tensions and subcutaneous tissue calipers came from the American Child Health Association, while a wooden sliding caliper graduated in both centimeters and inches came from the Marine Compass Company.

All measurements were done next to the skin, the children being stripped, except in the case of the public school examinations. In the schools the children removed their outer clothing and loosened the underclothing, permitting calipers to be slipped underneath.

Head diameters for breadth were measured euryon to euryon, for length, glabella to opisthocranion, with spreading calipers.*

Face and ear measurements were done with the small, straight-arm, sliding calipers. Face length was measured from menton to nasion, or tip of the chin to the suture between the nasal and frontal bones. Face breadth was measured as the distance between the two zygomatic processes.

Ear length was measured from superaurale to subaurale, and ear breadth, from preaurale to postaurale.

Interpupillary space was measured from the center of each pupil with eyes fixed.

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*Anatomic landmarks follow Wilde's system of anthropometry:

1. Euryon—the two points opposite each other on the sides of the skull which form the termini of the line of greatest breadth.
2. Glabella—the most prominent point in the median line between the two eyebrow ridges, a little above the frontonasal sutures.
3. Opisthocranion—the point is anatomically an indefinite one, and is simply the posterior end of the maximum length line of the skull, drawn from the glabella; the point where the posterior leg of the compass rests when spanning the greatest length.
4. Superaurale—the highest point on the free margin of the ear.
5. Subaurale—the lowest point on the free margin (lobe) of the ear.
6. Preaurale—the most anterior point on the ear, directly opposite the postaurale. The line between the preaurale and the postaurale is at right angles to the ear length line.
7. Postaurale—the most posterior point on the free margin of the ear.

The neck circumferences were measured just above the thyroid cartilage, the spring handle tape being used.

Measurements of transverse chest were taken from the front with straight-arm calipers at the nipple level, the instrument being parallel to the floor. Readings were made during the middle phase of quiet respiration for chest diameters. Anterior and posterior chest diameters were made with the spreading curved arm calipers at the junction of the fourth rib with the sternum, the instrument parallel to the floor. This is the nipple level in boys and also in girls up to the age of complete development of the breasts, when the nipple level becomes variable.

Biacromial diameters were measured from the back while the hands were hanging straight to the sides. The sharp borders of the acromial processes were palpated from behind forward and measured firmly with the straight-arm calipers held parallel to the floor.

The biiliac diameter is considered the most important of the transverse diameters, since it is the best indicator of the width of the trunk. This measurement is not variable with posture or respiration and the landmarks are very definite. The biiliac diameter was measured from the front with the straight-arm calipers and using firm pressure to get as nearly as possible a skeletal or bony measurement of the widest flare of the iliac crest.

The indices calculated show up various body proportions and were calculated as follows:

Cephalic: head breadth divided by head length
Face: facial height divided by bizygomatic diameter
Ear: ear breadth divided by ear length
Neck: neck length divided by neck circumference
Chest: anteroposterior thoracic diameter divided by transverse thoracic diameter
Width-length: bieristal diameter divided by standing height.

The width-length index expresses width of the body in percentage of height or the relative width. This width-length index has been found to be the best single measure of body build.

Our observations include 5,760 children from the ages of six months to sixteen years, which gives us between three and four hundred at each age level. These are about evenly divided between boys and girls. Statisticians agree that this is a large enough series to give adequate annual deviations.

The number of cases is indicated at the top of each table by age-sex groups. The minimum and maximum, to show the smallest and largest observation made, indicate the range. The mean is the arithmetic mean and gives the average for the group of that particular measurement.

	Girls Age Under 1 NUMBER OF CASES 106			Girls Age 1 NUMBER OF CASES 163			Girls Age 2 NUMBER OF CASES 150			Girls Age 3 NUMBER OF CASES 148		
Cephalic Measurements	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA
Breadth	11.0– 13.0	12.0	0.72	11.5– 13.0	12.3	0.47	12.0– 14.0	12.9	0.68	12.0– 16.0	13.6	0.98
Length	13.0– 16.0	14.9	0.96	15.0– 17.0	15.9	0.76	15.0– 17.8	16.4	0.73	16.0– 18.0	16.8	0.69
Index	700.0– 850.0	806.0	40.00	750.0–850.0	791.0	0.04	650.0– 900.0	785.0	52.00	700.0–900.0	812.0	50.00
Facial Measurements												
Height	5.0– 7.5	6.5	0.49	5.0– 8.5	7.1	0.59	7.0– 8.7	7.8	0.51	7.0– 9.0	8.1	0.72
Zygomatic diameter	9.0– 11.5	10.1	0.83	9.0– 11.5	10.3	0.42	9.0– 11.2	10.4	0.63	9.5– 11.2	10.6	0.57
Index	521.0–1064.0	709.8	77.00	454.0–762.0	646.3	80.00	636.0– 842.0	748.0	68.00	625.0–850.0	761.0	67.00
Ear Measurements												
Breadth	2.2– 3.0	2.5	0.16	2.2– 3.2	2.7	0.29	2.5– 3.5	2.8	0.30	2.5– 3.4	2.9	0.32
Length	4.0– 5.4	4.6	0.15	4.2– 5.2	4.7	0.42	4.2– 5.5	4.9	0.43	4.5– 5.7	4.9	0.36
Index	407.0– 667.0	544.3	59.40	532.0–750.0	597.2	70.20	519.0– 714.0	592.5	59.70	500.0–680.0	584.3	60.90
Interpupillary Space	4.0– 5.0	4.4	0.30	4.0– 5.5	4.5	0.43	4.0– 5.5	4.5	0.44	4.0– 5.5	4.6	0.41
Neck Measurements												
Length	3.5– 9.0	6.1	1.80	5.0– 10.0	7.7	1.60	7.0– 14.0	8.9	2.10	7.0– 13.0	9.0	1.30
Circumference	19.0– 28.0	22.5	2.80	20.0– 25.0	22.7	1.40	21.0– 26.0	23.0	1.60	22.0– 26.0	23.8	1.60
Index	159.0– 391.0	276.7	68.70	217.0–500.0	340.6	78.00	304.0– 538.0	387.1	63.90	260.0–545.0	411.6	69.60
Trunk Measurements												
Ant. post. thor. diam.	10.2– 13.0	11.4	0.99	11.0– 13.0	12.2	0.99	11.5– 14.0	12.6	0.88	11.5– 15.0	13.1	1.31
Lat. thor. diam.	11.0– 16.0	13.3	0.85	13.0– 16.0	14.7	1.15	13.0– 17.0	15.6	1.32	14.0– 18.0	16.1	0.97
Thor. index	637.0–1040.0	841.4		688.0–929.0	830.7		735.0–1000.0	811.5		765.0–914.0	812.1	49.00
Biiliac diam.	10.0– 14.0	11.6	1.07	11.0– 14.5	13.3	1.02	13.0– 16.2	14.4	1.18	14.0– 17.5	15.9	1.33
Biacrom. diam.	16.0– 20.0	17.8		18.0– 22.0	19.9		19.0– 27.0	22.4	2.21	21.0– 27.0	23.6	1.76
Width Length Index	150 – 190	175	7.95	150 –192	172	6.97	152 – 194	171	7.33	147 –188	168	7.30

	Girls Age 4 NUMBER OF CASES 163			Girls Age 5 NUMBER OF CASES 164			Girls Age 6 NUMBER OF CASES 170			Girls Age 7 NUMBER OF CASES 162		
	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA
Cephalic Measurements												
Breadth	12.0– 15.0	13.6	0.86	13.0– 15.0	13.7	0.68	13.0– 14.5	13.7	0.49	13.0– 14.5	13.9	0.51
Length	16.0– 18.0	17.2	0.62	16.0– 18.5	17.3	0.59	16.0– 19.0	17.3	0.71	16.0– 19.0	17.7	0.80
Index	700.0–850.0	786.0	50.00	700.0–850.0	793.0	39.00	700.0–850.0	789.0	38.00	700.0– 850.0	784.0	37.00
Facial Measurements												
Height	8.2– 10.0	8.9	0.56	7.0– 10.0	9.0	0.66	8.5– 10.0	9.3	0.40	8.5– 10.2	9.4	0.56
Zygomatic diameter	10.0– 13.0	10.8	0.79	10.0– 12.0	11.1	0.53	10.0– 12.0	11.0	0.59	8.0– 12.0	11.2	0.76
Index	769.0–950.0	830.3	49.30	636.0–905.0	795.5	68.70	772.0–972.0	865.2	57.90	756.0–1125.0	840.1	78.10
Ear Measurements												
Breadth	2.2– 3.3	2.8	0.35	2.2– 3.5	2.8	0.53	2.5– 3.4	2.8	0.26	2.5– 3.4	2.8	0.29
Length	4.5– 5.6	5.0	0.30	4.5– 7.0	5.2	0.58	4.7– 6.4	5.4	0.35	3.5– 6.2	5.4	0.59
Index	429.0–600.0	525.5	60.90	439.0–757.0	546.2	21.30	386.0–640.0	536.8	65.60	452.0– 850.0	540.7	62.40
Interpupillary Space	4.0– 5.4	4.7	0.51	4.0– 5.5	4.9	0.43	4.5– 5.5	5.1	0.27	4.5– 5.7	5.2	0.32
Neck Measurements												
Length	7.0– 12.0	9.2	1.20	8.0– 13.0	9.9	1.50	8.0– 14.0	10.7	1.90	9.0– 16.0	11.0	1.40
Circumference	22.0– 29.0	24.9	2.10	23.0– 28.0	24.9	1.60	20.0– 29.0	25.5	1.80	22.4– 29.0	27.2	1.80
Index	274.0–500.0	374.8	70.90	308.0–542.0	401.2	62.80	333.0–542.0	419.7	68.30	346.0– 666.0	452.6	98.90
Trunk Measurements												
Ant. post. thor. diam.	12.0– 17.0	13.4	1.17	12.0– 15.0	13.6	1.41	11.5– 17.0	14.2	1.36	13.0– 17.0	14.7	1.45
Lat. thor. diam.	15.5– 20.0	17.2	1.61	15.0– 19.2	17.4	1.33	16.0– 20.0	17.9	1.42	16.7– 21.0	18.5	1.38
Thor. index	684.0–900.0	780.6	48.10	686.0–880.0	782.9	48.90	664.0–909.0	783.2	47.20	675.0– 914.0	765.1	48.20
Biiliac diam.	15.5– 20.0	17.3	1.34	15.0– 20.0	17.6	1.36	16.0– 21.0	18.3	1.38	17.0– 22.0	19.0	1.54
Biacrom. diam.	22.0– 36.0	25.6	2.57	22.0– 30.0	26.8	2.26	24.0– 33.0	28.0	2.21	26.0– 35.0	29.6	2.64
Width Length Index	144 –184	164	7.84	144 –184	161	7.84	140 –180	159	8.42	144 – 174	159	7.63

	Girls Age 8 NUMBER OF CASES 173			Girls Age 9 NUMBER OF CASES 158			Girls Age 10 NUMBER OF CASES 232			Girls Age 11 NUMBER OF CASES 194		
Cephalic Measurements	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA
Breadth	13.0– 15.0	14.1	0.56	13.0– 15.0	14.1	0.49	13.4– 15.0	14.2	0.49	13.0– 15.5	14.3	0.62
Length	16.0– 19.0	17.8	0.71	16.2– 19.0	17.8	0.63	17.0– 19.0	17.9	0.63	17.0– 19.0	17.9	0.55
Index	722.0– 875.0	791.8	43.40	722.0–853.0	788.6	29.90	724.0– 833.0	790.7	26.40	722.0– 912.0	803.0	39.90
Facial Measurements												
Height	8.5– 10.7	9.8	0.52	9.0– 10.5	9.8	0.36	9.0– 11.0	10.2	0.62	9.8– 11.6	10.4	0.49
Zygomatic diameter	9.5– 12.5	11.5	0.78	10.0– 12.5	11.5	0.55	10.0– 13.0	11.8	0.63	10.0– 13.0	11.9	0.76
Index	708.0–1054.0	862.9	79.30	792.0–945.0	857.6	48.80	750.0–1110.0	868.9	66.70	800.0–1050.0	874.8	71.50
Ear Measurements												
Breadth	2.4– 3.5	2.8	0.26	2.3– 3.5	2.9	0.44	2.4– 3.4	2.9	0.31	2.4– 3.5	2.9	0.31
Length	4.7– 6.5	5.6	0.44	4.7– 6.3	5.6	0.49	5.0– 6.4	5.7	0.42	5.2– 6.5	5.7	0.42
Index	400.0– 600.0	499.0	45.60	444.0–648.0	553.8	54.30	421.0– 640.0	521.4	48.00	387.0– 577.0	499.7	53.90
Interpupillary Space	4.0– 5.7	5.2	0.41	4.8– 5.7	5.2	0.29	4.6– 6.0	5.4	0.35	4.7– 6.4	5.6	0.36
Neck Measurements												
Length	7.0– 15.0	11.2	2.00	7.0– 15.0	11.2	2.20	5.0– 17.0	11.3	2.30	8.0– 17.0	11.5	2.10
Circumference	23.0– 30.0	27.3	2.10	25.0– 31.0	27.5	1.50	26.0– 31.0	28.3	1.30	27.0– 33.5	29.0	1.40
Index	241.0– 549.0	416.4	82.90	241.0–536.0	392.6	79.90	185.0– 629.0	393.3	90.40	258.0– 531.0	390.1	75.70
Trunk Measurements												
Ant. post. thor. diam.	12.5– 17.5	14.8	1.24	13.0– 18.0	14.9	1.31	13.0– 18.5	15.3	1.51	13.5– 20.0	16.4	1.75
Lat. thor. diam.	17.0– 22.0	19.1	1.19	18.2– 23.0	19.9	1.89	19.0– 24.0	20.8	1.62	18.0– 27.2	22.0	2.03
Thor. index	650.0– 944.0	776.2	55.12	650.0–900.0	754.0	60.20	619.0– 842.0	747.9	52.20	537.0– 889.0	738.2	58.00
Biiliac diam.	18.0– 22.0	20.3	1.56	18.5– 23.0	21.1	1.97	20.0– 26.5	22.1	1.72	20.0– 29.5	23.1	1.84
Biacrom. diam.	22.0– 34.0	30.8	2.38	26.0– 34.0	31.1	2.31	28.0– 38.0	32.2	2.11	29.0– 38.0	33.0	2.58
Width Length Index	140 – 174	159	7.49	142 –174	159	6.11	134 – 185	160	9.85	140 – 185	161	8.90

	Girls Age 12 NUMBER OF CASES 258			Girls Age 13 NUMBER OF CASES 265			Girls Age 14 NUMBER OF CASES 183			Girls Age 15 NUMBER OF CASES 151		
Cephalic Measurements	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA
Breadth	13.0– 15.5	14.4	0.64	13.0– 16.0	14.4	0.40	14.0– 16.0	14.5	0.33	14.0– 15.5	14.6	0.52
Length	16.2– 20.0	18.4	0.88	17.0– 20.0	18.4	0.72	17.0– 20.0	18.5	0.73	18.0– 20.0	18.6	0.60
Index	700.0– 872.0	777.3	44.70	710.0–889.0	775.4	44.00	737.0–842.0	781.6	35.80	710.0–838.0	776.3	47.00
Facial Measurements												
Height	10.0– 11.0	10.5	0.43	9.8– 11.7	10.7	0.47	10.5– 11.5	10.8	0.52	10.0– 11.8	11.0	0.54
Zygomatic diameter	11.0– 13.0	11.9	0.76	10.5– 14.0	12.1	0.34	12.0– 14.0	12.8	0.75	12.0– 14.0	12.8	0.44
Index	800.0–1000.0	899.2	74.70	826.0–973.0	888.4	55.20	800.0–895.0	850.2	30.60	833.0–943.0	884.9	34.60
Ear Measurements												
Breadth	2.4– 3.5	2.9	0.29	2.4– 3.4	2.9	0.35	2.4– 3.5	2.9	0.25	2.3– 3.5	2.9	0.27
Length	5.0– 6.4	5.8	0.35	5.2– 6.2	5.8	0.34	5.0– 6.5	6.0	0.15	5.4– 6.9	6.0	0.30
Index	450.0– 648.0	521.8	65.50	403.0–597.0	516.9	62.20	450.0–533.0	466.5	38.60	404.0–593.0	504.4	46.00
Interpupillary Space	4.8– 6.5	5.7	0.43	4.7– 6.4	5.7	0.45	4.6– 6.4	5.9	0.32	4.3– 6.4	5.9	0.44
Neck Measurements												
Length	8.0– 20.0	12.6	3.30	9.0– 17.0	12.8	2.90	9.0– 20.0	14.2	3.50	9.0– 17.0	14.2	2.40
Circumference	27.0– 35.0	29.1	1.60	28.0– 33.0	30.5	0.80	29.0– 33.0	31.2	1.10	30.0– 34.0	32.1	1.20
Index	296.0– 645.0	432.4	114.10	300.0–429.0	370.1	40.00	290.0–645.0	465.5	115.9	265.0–550.0	443.7	86.10
Trunk Measurements												
Ant. post. thor. diam.	13.2– 22.0	16.7	1.81	14.0– 20.5	16.7	1.71	15.0– 23.0	17.8	1.81	14.2– 23.0	17.9	2.13
Lat. thor. diam.	20.0– 26.5	22.1	1.76	20.5– 29.0	24.1	2.04	19.0– 28.0	24.9	1.75	22.0– 28.0	24.9	1.93
Thor. index	604.0– 950.0	743.5	50.00	638.0–773.0	694.1	46.10	771.0–861.0	794.3	49.90	600.0–863.0	730.4	41.10
Biiliac diam.	20.0– 32.0	24.1	2.35	19.0– 29.0	25.1	2.12	20.0– 29.5	25.8	2.13	21.0– 31.5	26.2	2.39
Biacrom. diam.	30.0– 40.0	35.5	2.26	29.0– 39.0	35.9	2.19	28.0– 43.0	35.9	2.43	33.0– 40.0	36.2	1.96
Width Length Index	139 – 184	162	9.21	143 –189	163	10.46	139 –185	163	11.07	141 –184	164	9.65

	Boys Age Under 1 NUMBER OF CASES 109			Boys Age 1 NUMBER OF CASES 170			Boys Age 2 NUMBER OF CASES 154			Boys Age 3 NUMBER OF CASES 162		
Cephalic Measurements	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA
Breadth	12.0– 14.0	12.7	0.64	12.0– 14.0	13.2	0.71	12.0– 15.0	13.6	1.04	13.0– 14.5	13.8	0.56
Length	14.0– 16.0	15.3	0.56	15.0– 18.0	16.4	0.97	16.0– 19.0	17.0	0.95	16.0– 18.0	17.3	0.66
Index	700.0–900.0	826.0	70.00	700.0–900.0	806.0	64.00	650.0–850.0	798.0	59.00	700.0– 850.0	786.0	52.00
Facial Measurements												
Height	5.0– 8.0	6.7	0.57	7.0– 8.5	7.4	0.45	7.0– 9.5	8.1	0.55	7.0– 9.5	8.4	0.61
Zygomatic diameter	9.0– 12.0	10.2	0.74	9.0– 12.0	10.4	0.82	10.0– 11.5	10.6	0.42	10.0– 12.0	10.8	0.64
Index	583.0–889.0	698.2	82.90	540.0–800.0	677.6	81.80	666.0–863.0	738.7	80.90	636.0–1089.0	792.3	79.00
Ear Measurements												
Breadth	2.1– 3.5	2.6	0.16	2.5– 3.3	2.8	0.28	2.5– 3.4	2.9	0.34	2.5– 3.4	2.9	0.29
Length	4.2– 5.5	4.7	0.12	4.2– 5.5	4.9	0.38	5.0– 5.5	5.2	0.17	4.5– 6.0	5.2	0.48
Index	420.0–643.0	556.1	59.40	475.0–714.0	582.4	60.60	454.0–686.0	569.0	24.00	500.0– 666.0	572.8	57.60
Interpupillary Space	4.0– 5.2	4.6	0.27	4.2– 5.2	4.7	0.38	4.5– 5.5	4.7	0.34	3.7– 6.0	4.8	0.67
Neck Measurements												
Length	5.0– 10.0	6.8	1.62	5.0– 14.5	8.7	2.40	7.0– 11.0	8.7	1.20	5.5– 12.0	8.8	2.10
Circumference	20.0– 27.0	22.8	1.82	21.0– 27.0	23.7	2.30	21.5– 26.0	24.0	1.00	22.0– 29.0	25.0	2.00
Index	185.0–454.0	302.7	73.00	208.0–537.0	369.5	96.10	274.0–478.0	385.0	69.30	220.0– 500.0	352.0	72.10
Trunk Measurements												
Ant. post. thor. diam.	10.0– 12.0	11.2	0.63	10.2– 14.0	12.3	0.90	11.2– 14.5	12.5	1.46	12.0– 15.0	13.6	1.08
Lat. thor. diam.	12.0– 15.0	13.6	0.95	14.0– 17.2	15.2	1.58	15.0– 18.0	16.1	1.47	15.0– 19.0	16.6	1.37
Thor. index	632.0–936.0	804.6		639.0–933.0	813.5		700.0–900.0	804.1		609.0– 906.0	807.2	
Biiliac diam.	11.0– 14.2	12.2	1.06	11.0– 14.0	13.1	1.19	13.0– 16.0	14.5	1.56	14.0– 18.0	16.0	1.33
Biacrom. diam.	16.0– 27.0	18.7		18.0– 23.0	20.5	1.50	20.0– 23.0	21.9	2.64	22.0– 30.0	24.0	1.91
Width Length Index	155 –190	173 .	7.33	150 –190	168	6.54	146 –184	167	6.98	145 – 190	166	7.20

	Boys Age 4 NUMBER OF CASES 153			Boys Age 5 NUMBER OF CASES 161			Boys Age 6 NUMBER OF CASES 175			Boys Age 7 NUMBER OF CASES 163		
Cephalic Measurements	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA
Breadth	13.0– 15.0	14.1	0.64	12.5– 15.0	14.1	0.84	13.0– 15.0	14.2	0.51	13.0– 15.0	14.2	0.70
Length	16.0– 19.0	17.9	0.82	16.0– 20.0	18.0	1.09	17.0– 19.0	18.1	0.83	16.0– 20.0	18.1	1.02
Index	700.0–800.0	790.0	37.00	650.0–800.0	776.0	39.00	700.0–850.0	787.0	44.00	700.0–900.0	794.0	52.00
Facial Measurements												
Height	7.0– 9.5	8.9	0.50	8.5– 9.7	9.1	0.34	9.0– 11.0	9.8	0.44	8.5– 10.7	9.9	0.47
Zygomatic diameter	10.7– 12.0	11.1	0.71	10.0– 12.0	11.1	0.57	10.0– 12.0	11.4	0.68	11.0– 12.0	11.4	0.38
Index	727.0–940.0	799.1	71.20	708.0–920.0	835.6	65.40	792.0–955.0	868.9	46.30	713.0–945.0	859.0	57.60
Ear Measurements												
Breadth	2.7– 3.2	2.9	0.24	2.5– 3.1	2.9	0.23	2.7– 3.8	3.1	0.31	2.7– 3.6	3.1	0.27
Length	5.0– 6.0	5.4	0.28	4.3– 5.5	5.4	0.37	4.0– 6.4	5.6	0.53	4.5– 6.2	5.7	0.45
Index	474.0–600.0	546.5	48.50	500.0–721.0	568.2	69.80	469.0–680.0	563.3	56.50	435.0–607.0	542.4	47.30
Interpupillary Space	3.7– 6.0	4.9	0.48	4.5– 6.0	5.1	0.50	4.5– 6.0	5.1	0.41	4.5– 5.7	5.2	0.37
Neck Measurements												
Length	6.0– 13.0	8.9	2.10	6.0– 14.0	10.1	2.20	7.0– 14.0	10.3	1.60	8.0– 14.0	11.4	1.50
Circumference	24.0– 29.0	26.0	0.90	24.0– 27.5	26.3	1.70	24.5– 29.0	26.6	1.30	25.0– 29.0	26.7	1.40
Index	231.0–481.0	337.6	71.00	240.0–541.0	393.9	79.90	269.0–500.0	389.4	59.90	320.0–537.0	429.8	66.70
Trunk Measurements												
Ant. post. thor. diam.	12.0– 15.0	14.0	1.22	13.0– 15.5	14.5	1.20	13.2– 16.0	14.7	1.15	13.0– 16.0	14.9	1.31
Lat. thor. diam.	15.2– 20.0	17.6	1.10	15.0– 22.0	17.8	1.44	17.5– 21.0	18.8	1.61	17.0– 21.0	19.8	1.34
Thor. index	666.0–882.0	796.0		633.0–933.0	800.3	48.20	695.0–895.0	786.1	60.20	684.0–882.0	785.0	55.40
Biiliac diam.	15.0– 19.5	17.2	1.26	16.5– 20.0	18.1	1.28	16.2– 22.0	18.5	1.67	17.0– 21.2	19.3	1.55
Biacrom. diam.	20.0– 32.0	25.9	2.39	23.0– 29.0	26.2	1.77	26.0– 32.0	29.0	2.48	25.0– 36.0	30.0	2.43
Width Length Index	139 –180	162	7.20	139 –190	161	7.27	139 –180	160	6.76	145 –174	159	6.48

	Boys Age 8 NUMBER OF CASES 166			Boys Age 9 NUMBER OF CASES 157			Boys Age 10 NUMBER OF CASES 218			Boys Age 11 NUMBER OF CASES 193		
Cephalic Measurements	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA
Breadth	13.0– 15.0	14.3	0.38	13.5– 15.0	14.4	0.51	13.0– 15.0	14.6	0.41	13.4– 16.0	14.6	0.73
Length	17.0– 19.2	18.2	0.52	17.0– 19.0	18.2	0.63	17.2– 20.0	18.3	0.62	17.0– 19.5	18.5	0.74
Index	733.0–834.0	787.8	24.70	765.0– 880.0	793.1	33.90	700.0–843.0	796.6	36.30	705.0–889.0	783.9	50.00
Facial Measurements												
Height	9.2– 11.0	10.1	0.59	9.5– 11.0	10.1	0.48	9.7– 11.7	10.5	0.59	9.7– 11.6	10.5	0.50
Zygomatic diameter	11.0– 12.4	11.7	0.55	11.0– 12.5	11.8	0.76	11.0– 13.0	12.2	0.71	11.0– 14.0	12.4	0.59
Index	767.0–945.0	866.7	60.10	832.0–1000.0	882.7	75.00	808.0–955.0	857.1	59.10	770.0–917.0	812.8	61.50
Ear Measurements												
Breadth	3.0– 3.4	3.1	0.20	2.8– 3.5	3.1	0.17	2.7– 3.4	3.1	0.20	2.8– 4.5	3.1	0.51
Length	5.0– 6.7	5.9	0.45	5.0– 6.2	5.9	0.38	5.5– 6.7	5.9	0.33	5.0– 7.0	5.9	0.32
Index	477.0–600.0	522.8	36.40	500.0– 600.0	542.0	33.70	448.0–545.0	505.1	26.20	429.0–750.0	540.1	96.00
Interpupillary Space	4.5– 6.2	5.3	0.51	4.5– 6.2	5.5	0.36	4.7– 6.2	5.5	0.47	4.7– 6.2	5.5	0.46
Neck Measurements												
Length	8.0– 14.0	11.2	2.20	9.0– 13.0	11.0	0.30	8.0– 14.0	11.9	2.30	8.0– 16.0	12.2	3.00
Circumference	24.0– 33.0	27.6	2.10	25.0– 32.0	28.5	2.20	27.0– 35.0	29.8	2.30	28.0– 33.0	29.9	1.40
Index	233.0–500.0	362.9	84.30	312.0– 500.0	401.2	54.20	281.0–481.0	366.6	65.30	256.0–571.0	409.0	99.80
Trunk Measurements												
Ant. post. thor. diam.	14.0– 18.0	15.7	1.28	13.0– 17.0	15.8	1.19	14.5– 19.0	16.7	1.55	15.0– 19.5	16.7	1.52
Lat. thor. diam.	18.0– 28.0	20.1	2.20	18.0– 23.0	20.6	1.83	18.0– 25.5	21.7	1.57	18.0– 25.0	21.9	1.55
Thor. index	700.0–895.0	780.7	50.90	650.0– 944.0	755.9	51.80	640.0–857.0	775.2	51.00	660.0–944.0	784.3	58.70
Biiliac diam.	18.0– 22.5	20.3	2.02	19.0– 25.0	21.1	2.30	19.0– 24.8	21.6	1.63	20.5– 26.0	22.3	1.75
Biacrom. diam.	29.0– 37.0	31.9	2.71	28.0– 36.0	32.5	2.64	30.0– 41 0	34.4	2.40	30.0– 40.0	34.8	2.52
Width Length Index	140 –178	158	7.32	140 – 180	157	6.49	134 –180	158	7.80	139 –184	157	7.59

	Boys Age 12 NUMBER OF CASES 260			Boys Age 13 NUMBER OF CASES 264			Boys Age 14 NUMBER OF CASES 106			Boys Age 15 NUMBER OF CASES 119		
Cephalic Measurements	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA	RANGE	MEAN	SIGMA
Breadth	13.0– 15.5	14.7	0.56	13.5– 16.0	14.7	0.77	13.4– 16.2	14.8	0.52	13.0– 16.0	15.0	1.41
Length	17.0– 20.0	18.5	0.78	17.0– 20.0	18.5	0.78	17.0– 20.0	18.6	0.54	17.0– 20.0	18.7	0.45
Index	725.0– 872.0	781.7	37.90	737.0–941.0	797.3	81.40	692.0–790.0	739.7	32.20	789.0–823.0	800.5	45.70
Facial Measurements												
Height	10.0– 12.0	10.5	0.50	10.0– 12.0	10.8	0.50	10.4– 12.0	11.3	0.59	10.5– 12.0	11.3	0.68
Zygomatic diameter	11.0– 13.5	12.6	0.61	11.0– 15.0	12.8	0.79	12.0– 14.0	13.0	0.71	12.0– 14.0	13.0	0.63
Index	832.0–1000.0	905.5	74.70	733.0–955.0	859.6	59.80	857.0–960.0	908.3	33.40	808.0–875.0	850.5	20.80
Ear Measurements												
Breadth	2.5– 4.0	3.1	0.53	3.0– 3.5	3.2	0.23	3.0– 3.4	3.2	0.23	2.7– 3.5	3.2	0.33
Length	5.2– 6.5	5.9	0.48	5.4– 7.0	5.9	0.40	6.0– 7.4	6.3	0.50	6.2– 7.0	6.3	0.26
Index	308.0– 615.0	489.5	96.20	476.0–618.0	531.9	36.20	422.0–548.0	483.3	40.10	435.0–531.0	470.2	48.00
Interpupillary Space	4.5– 6.0	5.5	0.41	5.2– 6.4	5.6	0.35	5.2– 6.0	5.6	0.36	5.2– 6.5	5.9	0.52
Neck Measurements												
Length	9.0– 16.8	12.3	2.20	7.0– 17.0	12.5	2.40	10.0– 16.5	13.3	2.50	10.0– 15.0	12.8	2.50
Circumference	27.5– 31.0	30.3	3.30	25.0– 36.0	30.6	2.50	32.0– 36.0	33.1	2.40	30.0– 39.0	35.0	3.00
Index	305.0– 600.0	409.0	82.80	269.0–531.0	410.3	74.40	312.0–500.0	405.7	81.80	279.0–466.0	373.5	63.20
Trunk Measurements												
Ant. post. thor. diam.	14.5– 19.0	16.9	1.54	15.0– 21.0	17.8	2.20	18.0– 24.0	20.1	2.49	17.0– 27.0	21.7	2.09
Lat. thor. diam.	19.0– 23.0	21.9	1.68	20.0– 28.5	23.4	2.41	22.0– 29.0	25.4	2.43	22.0– 30.0	26.8	2.28
Thor. index	652.0– 905.0	753.0	55.20	500.0–909.0	765.7	56.40	714.0–845.0	793.0	55.40	600.0–808.0	731.7	60.80
Biiliac diam.	21.0– 25.0	23.1	1.52	21.0– 32.0	23.6	1.89	21.5– 28.5	24.9	2.14	24.0– 31.5	25.4	2.43
Biacrom. diam.	32.0– 37.5	35.9	2.54	33.0– 42.0	36.9	1.74	35.0– 40.0	38.3	2.62	36.0– 43.5	38.6	2.55
Width Length Index	140 – 175	157	7.21	144 –180	156	7.84	139 –180	156	7.25	135 –184	155	8.06

The sigma or standard deviation is the most important constant, since it shows the amount of variation around the average. The word "normal" has ceased to mean "average" and has taken on rather the meaning of falling into certain ranges or zones of variation from average. Porter[24] in 1893 recognized it when he said the average was "that value which is as often exceeded as attained."

Standard deviations help to mark off these zones of normality. The zone included between one standard deviation plus and one standard deviation minus the average, takes in 67 per cent of the general population, leaving 16.5 per cent to vary more than one standard deviation in either direction. This will be true of any series of biologic data which is large enough to give statistical constants.

For purposes of designating an arbitrary line in classifying children, we have used the standard deviation as a convenient unit of measure because of the mathematical and statistical logic of this unit.

Hejinian and Hatt[25] stressed the importance of measuring the variation within, as well as the central tendency of, the age group in interpreting body measurements in young children.

Having fulfilled the statistical requirements for number of cases and homogeneity, we feel that comparing physical measurements of a given child of similar social status with this series should indicate something of his consistency of development. In other words, it should show up his disharmonies if he fell within one zone for chest development and another zone for lower trunk development.

The child whose physical traits all fell within the same zone, who varied from the average in the same direction and approximately the same amount for his different traits, would be classified as normal whether he were much smaller than average or much larger than average.

The importance of indices is seen when intepreting absolute measurements which vary markedly from the average in either direction. Interpretation depends upon relative size and not upon absolute size. Thus a child whose chest or pelvic measurements were very small may be found to be short in stature too, consequently making his body proportions normal. Conversely, if the transverse diameters are very large and the child is found to be taller than average, his body proportions may be very similar to the short child with narrow diameters. Indices compare the relative build of a child with others of his own age sex group or with those of different ages equally well.

Indices also show up the interrelationship of various body proportions to the others in the same child; i.e., a child may have a relatively small chest and a relatively large head.

Boas[26] found that:

A. Variability of annual growth increased with age.

B. Young children grow more uniformly than older ones.

C. Variability is greatest during adolescence.

D. Growth of girls is more variable than that of boys.

These four points are all confirmed and demonstrated in our tables.

Boas concluded that during the early years of childhood short children grow more slowly than tall children. During adolescence they continue to grow, while tall children have more nearly reached their full development. Smallness may therefore be due to slowness of development.

Differences in development between various social classes are, to a great extent, results of acceleration and retardation of growth which act in such a way that the social groups which show higher values of measurement do so on account of accelerated growth, and they cease to grow earlier than those whose growth is in the beginning less rapid, so that there is a tendency to decreasing differences between these groups during the last years of growth.

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THE EFFECT OF PLACENTAL EXTRACT ON THE DICK TEST

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IN 1933 McKhann and Chu[1] reported the successful separation from the human placenta of an extract composed largely of pseudoglobulins which they showed to have several important immunologic properties. Among these was the ability to blanch scarlet fever rashes, in some instances more effectively than scarlet fever antitoxin. Despite the fact that there is considerable uncertainty about the immunologic aspects of scarlet fever and the relation of the Dick toxin to it, it seems fairly definitely established as the result of the work of the Dicks and others that most individuals exhibiting a positive Dick test are susceptible to scarlet fever and that the test may be regarded as a quantitative as well as a qualitative measure of the degree of susceptibility to the disease.

It was thought therefore that some light might be shed on the action of the placental extract if one were to administer it to a group of children who reacted positively to the Dick test and follow this administration by repeated Dick tests at frequent intervals, considering any variation in the size of the reaction as an indication of changed levels of immunity to scarlet fever. This would seem particularly interesting in the absence of any published work on the use of the extract in preventing scarlet fever in exposed susceptible subjects, similar to its use already reported in measles.

The study was undertaken on fifteen children being treated for orthopedic conditions in the Shriners' Hospital for Crippled Children, who were found to react positively to the Dick toxin as prepared by the Connaught Laboratories, Toronto. None of these patients had had scarlet fever. Their ages varied from fifteen months to fourteen and one-half years. The placental extract was administered intramuscularly in single doses of 5 c.c. or 10 c.c.

In most cases there were complaints of considerable discomfort at the site of injection for several hours. In no instance was there fever or other evidence of systemic reaction.

The precautions suggested by the Dicks[2] to assure accurate readings were observed. The tests were read in twenty-four hours and measured carefully by the author. In the event of oval reactions the mean of the length and breadth was considered as the diameter.

From the Henry J. Elliott Research Fund of the Shriners' Hospital for Crippled Children, Montreal Unit.

The controls consisted of five children with positive Dick tests, chosen at random; to these no extract was given.

Chart 1 shows graphically the effect of the extract on the Dick tests of these children. Table I gives the dosages, ages, etc. It will be seen that the controls remained relatively unchanged by the repeated injections of toxin, at least over the period of observation. All the children who received extract showed a tendency to become almost or definitely Dick-negative in a few days, with a tendency to become Dick-positive again in a varying period. Eight of the fifteen reached or fell below the

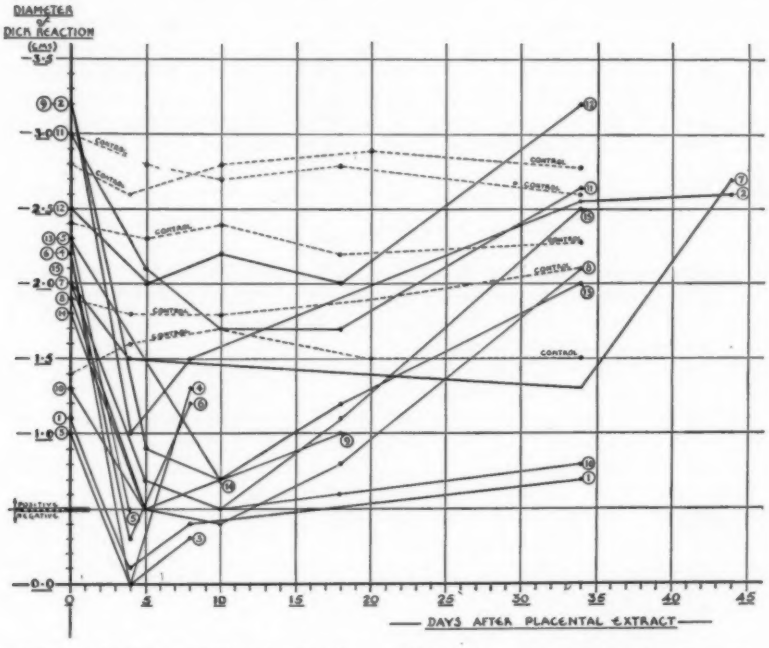

Chart 1.—Showing variations in the size of Dick tests made at intervals after administration of placental extract to fifteen Dick-positive children.

level (0.5 cm.) generally considered the borderline between positive and negative Dick tests. The amount of material administered and the age of the patient bore no relation to the rapidity of fall in the curves, the level to which they returned, or the rate of return.

Interpreting these findings in terms of immunity to scarlet fever, one may say that the placental extract* used in this study in a small series of children was able to produce, in the majority of cases, rapid reduction

*The placental extract used in this study was kindly furnished by E. R. Squibb & Sons.

in the susceptibility to scarlet fever as indicated by the changing of a positive Dick test into a negative one.

TABLE I

THE AGE AND SEX OF PATIENT AND LOT NUMBER AND DOSAGE OF EXTRACT ADMINISTERED

PATIENT	AGE IN YR.	SEX	EXTRACT LOT NO.	DOSE	HOSP. NO.
A. S.	2 6/12	M	51944	5 c.c.	1691
M. C.	6 9/12	F	51944	5 c.c.	1792
A. D.	1 3/12	M	51944	5 c.c.	1782
R. B.	3 5/12	M	51944	5 c.c.	1714
N. A.	4 6/12	M	51944	5 c.c.	1399
F. K.	11	M	51944	5 c.c.	791
C. M.	8 6/12	M	51944	5 c.c.	1639
M. M.	11 4/12	M	51944	10 c.c.	1858
V. G.	9	M	51944	10 c.c.	1865
C. J.	2 4/12	M	52404	5 c.c.	1835
N. S.	13	F	52404	10 c.c.	1816
H. K.	7 3/12	F	52404	10 c.c.	1709
M. R.	10 8/12	F	52404	10 c.c.	1722
N. L.	2 5/12	F	52404	5 c.c.	1841
B. B.	14 5/12	F	52404	10 c.c.	937

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DRUMMOND MEDICAL BUILDING

Pediatric Clinics

THE CHILDREN'S DEPARTMENT OF THE LONDON HOSPITAL, ENGLAND

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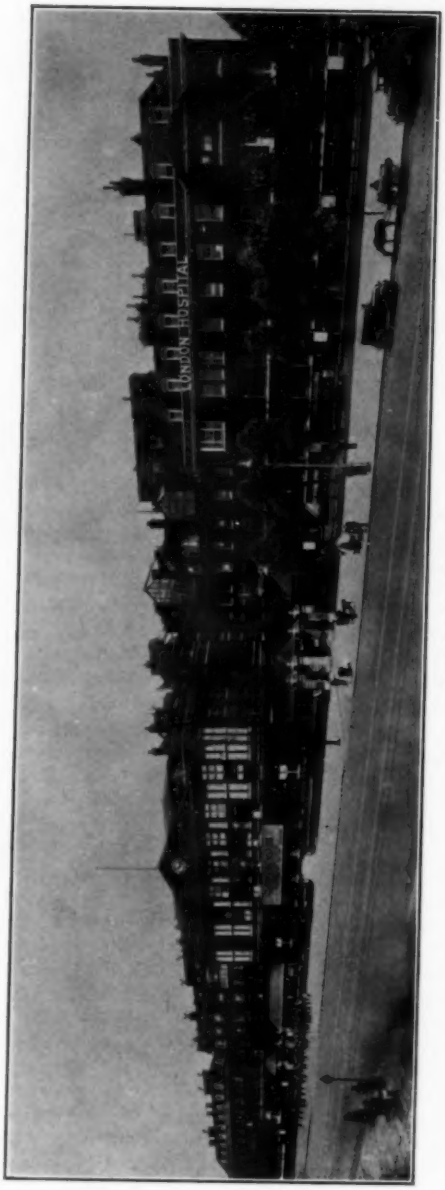
THE London Hospital, which is the largest voluntary and teaching hospital in England, is situated in Whitechapel, in the east end of London, one of the poorest and most crowded sections of the city. It has a total of 856 beds, and the out-patient attendances number approximately 10,000 per week. As may be imagined, the wealth of clinical material is unrivalled, for, apart from the mere question of numbers, the Hospital draws not only from the east end of the city but also from the whole of the Thames dock areas, and from the districts running down to the southeast coast of England.

When one considers the size of this hospital, it may appear surprising that the formation of a special children's department was a comparatively recent development. In this respect the London Hospital is not, however, backward among general hospitals in this country, for the formation of children's departments in the English teaching hospitals is really a postwar development. Prior to 1918 such departments were most exceptional, and their formation in some hospitals has occurred only very recently. There are still large teaching hospitals in London without special children's departments, although, of course, children are treated in these hospitals. The reason for the comparatively recent inauguration of these special departments is to be found in the fact that the medical profession in England has viewed such specialisation with some misgiving, owing to its inherent disadvantages. So far as paediatrics is concerned, it has been felt that the general physician is a proper and competent person to deal with the sick child; that were he to relinquish this work, his medical knowledge and experience would suffer as a result of his being divorced from the opportunity of seeing disease in some of its early phases peculiar to childhood; that on the other hand the man who dealt purely with children would have his outlook limited and his experience curtailed—at any rate in regard to prognosis—by losing sight of his patients after they had attained a certain age. That this attitude is an understandable one nobody can deny. There are, however, manifest advantages in having a purely paediatric department, and the patient, in particular, would seem on the whole to reap the benefit of being under the care of a physician specially trained and experienced in paediatrics. One may state that this principle is now as firmly established here as abroad. This is shown by the fact that special children's departments have come into being in most of the large general teaching hospitals. In these there is the special advantage that the paediatrician, owing to contact with his colleagues and to the proximity of adult patients, is certainly less likely to lose touch with general medicine than might be the case if he were working exclusively in a children's hospital.

It was at the commencement of 1921 that the first move was made toward the formation of a special children's department in the London Hospital. Till then, children had been treated as out-patients and inpatients by the general physicians to the hospital without special segregation, although two children's medical wards,



The London Hospital

with a total of forty-two beds, had been set apart for patients up to the age of seven years. (This age limit has recently been raised to twelve years.) At the date above mentioned, the Medical Council recommended that in the interests of all concerned a special treatment centre for the care of infants and children under five years of age should be instituted within the Hospital. The Hospital Committee agreed with this recommendation, and consequently a special out-patient session for young children was inaugurated; Dr. Charles Miller, a physician already on the hospital staff, was selected as being peculiarly suited for taking charge of the new venture. It was not, however, until a few years later that a true children's department was instituted. In 1925 Dr. A. G. Maitland-Jones, who had previously assisted Dr. Miller, was appointed to the honorary staff of the hospital as physician in charge of the children's department, and this department, designed to deal with children from infancy to school-leaving age, commenced its work in July, 1926. Like its fellows in other English hospitals, the department constituted a unit for dealing with the care, management, and *medical* diseases of infants and children. Children suffering from surgical conditions, on the other hand, were dealt with as previously along with the general surgical patients, although for inpatients there were as heretofore two children's surgical wards.

The children's department commenced its work with out-patients in accommodation which, although possible, was by no means ideal. At first two morning sessions a week were devoted to the work, but very soon a third was added, in which only old patients were seen. Shortly after the opening of the out-patient clinic, one of the children's wards of twenty-one beds was completely taken over by the department, and a little later five beds in adult wards, available for children up to sixteen years of age, were allotted to it. The importance of this latter arrangement lies in the necessity for being able to admit to hospital any children attending the out-patient clinic, without being confined to the age limit required for admission to the children's ward. It may be asked why only one of the two children's medical wards was taken over in forming a special department. The reason for this is that hitherto the beds in both wards had been shared by the general physicians to the hospital, and in order to avoid severing their connection with children entirely, it was decided that only one ward should be allotted to the newly formed children's department and that the beds in the other ward should be shared as before among the general physicians, who could thus, to the advantage of themselves and of their house physicians (resident medical officers), keep in touch with medical conditions peculiar to childhood. The beds in this ward are kept filled by cases demanding urgent admission to the hospital on certain days of the week, while the children's department ward draws its patients from its own out-patient department (to which all children requiring out-patient treatment are referred) and from emergency admissions on the remaining days of the week.

In addition to the physician-in-charge, the staff of the department consisted at the outset of a first assistant, a resident house physician, and two clinical assistants. The work grew with great rapidity, and expansions in various directions were required. In 1930 an entirely new set of rooms was erected to our requirements and design, the whole layout of waiting rooms, dressing and weighing rooms, and rooms for consultation and treatment being planned to meet the special needs of the department. In 1931 Dr. K. H. Tallerman, till then first assistant, was elected to the honorary staff of the hospital as assistant physician to the department. Dr. R. W. B. Ellis was appointed to take his place as first assistant and registrar.

With the expansion of staff the activities of the department have been still further extended, and at the present time the work is carried on in the following manner.

An out-patient clinic works on four mornings a week. There is the care of twenty-six inpatient beds for children up to fourteen years of age who are suffering from medical diseases. There is supervision and care of all infants in the obstetric nurseries. A follow-up clinic is conducted once weekly for newborn infants delivered either in the obstetric wards or by nurses or students of the Hospital attending the mothers in their own homes (a regular part of the English obstetric training). The infants attend at this clinic until the age of two months, when, if progressing normally, they are transferred with a brief written report to the municipal clinics in their own district. These municipal clinics are responsible to the Ministry of Health for operating the national maternity and child welfare scheme, and have an organisation including home visiting by nurses, which is beyond the scope of hospital work in its ordinary sense. Infants who at the age of two months are considered to be in any way abnormal are not referred in this way to their local welfare clinics but are transferred to the ordinary sessions of the children's department, where they are treated until fit for discharge from hospital care. The relations with the above mentioned municipal clinics are very friendly, and our department acts as a consultation centre to these clinics, cases of difficulty being referred from them for consultative opinion and hospital treatment if necessary. There is in addition in the department a special clinic held once weekly for the investigation of breast-fed infants who fail to thrive. At this breast-feeding clinic there are facilities for test-weighing the infant at three successive feedings, while the mother may spend the day at the clinic. The average amount the infant is taking thus becomes known and is reported to the physician at the next ordinary attendance of the mother and child; complementary feedings or adjustments of the feeding can thus be accurately estimated. At this clinic the mother also receives instruction in the technique of breast feeding, by the sister in charge. Finally, there is in operation a clinic for the treatment of speech defects, tuition being carried out by two specially qualified workers in this field. The department also acts in a consultative capacity to the School Medical Service and treats if necessary any children referred by the school medical officers; through the agency of a special secretary, reports on such children are sent back to them. A social service worker is allotted to the department, and great help is afforded in the out-patient clinic by three or four voluntary workers.

A modified appointment system operates in the out-patient clinic, and although it is impossible, especially on account of student teaching, to see each patient at an individually arranged time, patients are allotted times for the subsequent visit and are booked in advance to attend in batches at hourly intervals. Thus the amount of waiting to which they are subjected is cut down very considerably.

The laboratory facilities at the Hospital are extensive, and, although no laboratory is set aside solely for the use of the paediatric department, full investigation of any case can always be obtained, and accommodation is allotted for any member of the department wishing to carry out any particular research work. The published work of an experimental character which has emanated from the department goes to show that such facilities have been appreciated and utilised. In the same way all the other special departments of the Hospital—x-ray, electrical, massage, etc.—offer every means for full investigation and treatment of cases and for consultation with colleagues engaged in other branches of medical work.

The mass of clinical material makes great opportunity for clinical research, and the facilities of the Hospital and the cooperation of members of the staff in other departments make this very fruitful. In recent years studies on the prognosis of nephritis and of obesity in childhood, on recurrent vomiting attacks in children, and on atelectatic bronchiectasis may be cited as examples of work of this character carried out in the department by members of its staff.

As one of the principal functions of a general teaching hospital is the training of medical undergraduates, it may be of interest to set out briefly the plan of paediatric teaching which is adopted. Instruction in regard to the infant and child is arranged to run concurrently with instruction in midwifery and obstetrics. During a two-month period in which the student is engaged in carrying out his practical midwifery, he is given an elementary course in infant feeding, receives instruction upon the newborn by means of ward rounds in the obstetric nursery conducted by a paediatrician, and further attends the infant follow-up clinic, where he has the opportunity of seeing again the patients he has delivered and of noting their progress and the methods adopted in handling such feeding difficulties that may arise. It seems a logical and advantageous arrangement that he should receive such instruction while learning obstetrics. At this time also he is given a weekly demonstration of patients in the children's medical ward, a preparation for his work as a ward clerk. During the three-month period following this, and while he is engaged also in gynaecology, he is appointed a clinical clerk in the children's department; as such he has allotted to him inpatient cases, of which he is expected to take a history, make the necessary examinations, and keep subsequent progress notes. This is of course additional to the examination and notes of such cases made and recorded by the resident-in-charge. During this period of clerkship, the student attends a weekly ward round or demonstration conducted by the physician in charge of the department and attends at a teaching session in the out-patient department conducted by the assistant physician to the department. A feature of the out-patient session is the teaching on unselected cases attending the department on that particular morning. By this means students have the opportunity of seeing how ordinary cases coming to hospital for a first visit are handled, of observing the methods adopted for arriving at a diagnosis, of learning what investigations may be required in any particular type of case, and, in fact, of getting to realise how any particular medical problem is handled in the way they will have to handle it themselves later in practice. In addition to such formal teaching, students are helped and supervised on their own cases in the ward by the first assistant to the department.

During their period of attendance in the department, it is arranged that students also attend a few sessions at an infant welfare centre conducted by a municipal authority, in order to gain an appreciation of the type of work carried out in such clinics, and to learn the methods of approaching infant management and feeding from a prophylactic standpoint.

Finally, a course of didactic lectures in paediatrics is held for the students during alternate winter sessions, and before qualifying in medicine each student is required to have attended such a course.

Realising the impossibility of giving an adequate training in any special branch of medicine to men during their student period, the whole object of the paediatric teaching in the department is to give at any rate a comprehensive survey of paediatric work from all angles, with insistence upon the common problems in the subject which are likely to crop up continually in a general practitioner's experience. To those who wish for more complete training in paediatrics, clinical assistantships and later the resident post of house physician are available.

It is encouraging to find how large a number of students attend the teaching sessions in the department after the days of their compulsory clerkship are over. In this way these men, who are always free to come to these sessions if they wish to, supplement the statutory course, which in the very nature of things is bound to be somewhat brief.

The department also takes its share in the postgraduate medical teaching of the hospital, demonstrations and lectures being given as part of a regular course held

twice in each year; any postgraduate attending the practice of the hospital is always welcomed in the department, should he care to attend at the ward rounds or the out-patient teaching sessions.

The case notes both for inpatients and for out-patients are kept in a manner similar to that employed at all up-to-date hospitals, and call for no special mention, except that it may be noted that for out-patients a folder system is adopted, and the case notes are comparable in completeness with those of the inpatients. They are never handled by the patients themselves; when an out-patient is admitted to the ward, the case folder goes to the ward too; subsequently a summary of the in-patient notes is made upon it by the house physician when the patient is discharged. Continuity between out-patient and in-patient notes is thus carried on in a useful and practical manner.

Criticism is sometimes levelled against the rapidity and the apparently casual methods of examination seen in English out-patient clinics. When, for example, it is considered that a limited staff, in the department above described, has to deal with approximately 15,000 attendances, including 2,000 new patients a year, it will be realised that the full working up of a case becomes entirely a function of the inpatient department. In the out-patient clinic one is called upon to handle and to teach upon a mass of quite unselected material and to deal with it in the same way in which a practitioner must handle a busy practice, seeding those cases which on clinical grounds require further or special investigation and dealing with them accordingly. In our view such a method enhances enormously the clinical experience of both student and staff, and in actual practice it does not appear to be disadvantageous to the patients themselves.

An attempt has been made in the above brief article to give an insight into the work and teaching methods of a paediatric department of a large English general teaching hospital. It was felt that such an account would be more interesting and more profitable than would be the case if attention had been centred chiefly upon any particular subjects of investigation being carried out in the department.

Critical Review

ALLERGIC DISEASES

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EXPERIMENTAL AND THEORETICAL CONSIDERATIONS

"THE manifestations of allergy are becoming more and more familiar to physicians. They are forced to take cognizance of variations in the reactions of living tissues to foreign chemical agents whether antigenic or nonantigenic in character, or whether the change is toward hypersensitivity or reduced sensitivity. The discovery of the substance responsible for the sensitization or intoxication often taxes the ingenuity of the medical observer to the utmost." This quotation from an editorial[1] in the *Journal of the American Medical Association* implies an importance hardly anticipated by the pioneers in the field. When the lack of parallel between animal experimental studies and human clinical observations is considered, the report on which the above comment was made is important.[2] It concerned the feeding problem of a baby walrus. When this animal was fed cow's milk, a rash quite similar to that seen in human beings developed. It could be relieved or produced at will by removing or administering the milk.

In the field of experimental studies the past year has brought several important contributions. Burky[3] was able to produce reactions of hypersensitivity in the rabbit to lens protein, ragweed extract, and even homologous muscle protein by combining the substances with staphylococcus toxin. This peculiar effect of a bacterial toxin's increasing antigenicity of substances is spectacular and may clarify our understanding of the development of new sensitizations in allergic individuals following infections. R. A. Cooke,[4] discussing Burky's report, suggested that a closer parallel with human allergy might result in experimental animals by introducing the inheritance factor with inbreeding and increasing sensitization, by infection and exposure to the antigens. Caulfeild,[5] of the Connaught Laboratories, in his discussion reported the precipitation of asthma after an interval of freedom when the patient was treated with staphylococcus toxoid for boils. Such episodes should make us cautious in using certain bacterial products on an asthmatic patient. Naturally, it does not follow that all infections will aggravate the allergic symptoms. Clinically, it is difficult to predict the effect of infections. The reviewer recalls two brothers of six and eight years, who had measles, one of whom had been asthmatic but was free from symptoms after the infection, while the other brother developed asthma for the first time while convalescing.

The allergic aspects of certain infectious diseases continue to aid in clarifying their clinical features. In Moore's[6] recent book on syphilis

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there is, for example, the discussion of the "allergic type" prone to develop gummatous lesions, the cardiovascular type, and one which has apparently attained degrees of resistance to *Treponema pallidum*. The allergic response is described as explosive though free from degenerative phenomena. Incidentally, Moore found no greater intolerance for arsphenamine in the patients who also had asthma or hay fever.

Wherry[7] discussed the rôle of desensitization in recovery from bacterial infection. He suggested, in addition to the active desensitization by bactericidal agents, a desensitizing serum for treatment of the acute phases comparable to the Foshay[8] serum for tularemia. Again, there is the challenge of Rich[9] (discussed in my previous critical review[10]), that the allergic reaction can hardly be considered as a beneficial penalty for relative immunity.

A brief report by Miller[11] deals with the specificity of allergic reactions to certain gram-negative diplococci. He found a close relationship between meningococci and gonococci in his work with rabbits, less crossing with catarrhalis, and apparently no common factor with *B. lepisepticum*.

A study of the anaphylactic antibody by Swineford[12] showed that it was present in both water-soluble and water-insoluble serum globulins. After producing passive sensitization of guinea pigs to horse serum by the use of a rabbit (horse-sensitive) antibody, protection was obtained by the use of both the water-soluble and the whole globulin fractions. The work of Cohen, Rudolph, Wasserman and Rogoff[13] is difficult to evaluate. They attempted to show the relation of the adrenal gland to allergic phenomena and were unable to detect any increased epinephrine output during anaphylactic excitation of the dog. Saunders, Holsinger and Cooper[14] described anaphylactic-like reactions produced by the streptococcus associated with gastric ulcer. They postulated a sensitization which might explain the periodicity of symptoms in some of the patients. The allergic (anaphylactic) theory of rheumatic infection was restated by Jenkins,[15] who felt there was no better explanation yet advanced for it. This tenet has been discussed in previous reviews.[16]

A peculiar experimental finding is that of Sulzberger and Simon[17] regarding guinea pig arsphenamine hypersensitivity. Failure to duplicate the findings in New York City, despite success in different localities elsewhere, spoke for some geographic factors, such as water. However, the main thesis of the work showed that the sensitivity did not depend on arsenic content but varied with the brand used. From this it would appear desirable to test the various lots of arsenic on guinea pigs to prevent, if possible, reactions in the human with arsphenamine therapy.

It will be recalled from previous reviews that Rackemann[18] had constantly resisted the tendency for too strict a classification which would separate animal (anaphylactic) from human allergic phenomena. This year, with Simon,[19] he has added further weight to his argument by inducing the hypersensitive state in man. While it is conceded that serum sickness, like the primrose (contact) dermatitis of Bloch,[20] can be induced, these studies seem to offer valuable information regarding the whole field of allergy. Rackemann and Simon obtained a sensitivity to guinea pig serum by repeated intracutaneous injections. Early

in the sensitization experiments the skin gave a delayed response, and later it developed the immediate wheal and erythema as in the usual allergic (atopic) skin test. The production varied definitely with the dosage of serum but was produced just as easily in allergic as in non-allergic individuals. Passive transfer of the skin test was successful in proportion to the intensity of the direct skin test. A second group of atopic individuals was sensitized by nasal administration. These experiments would seem most vital to anyone interested in theoretical discussions of allergy. While it is granted that serum sensitivity has certain differences from other types of sensitivity, this study of its production in man suggests parallels with Rhus dermatitis and related "contact" dermatoses in which the skin test is usually considered of no importance and the patch test, specific. It further suggests the significance of "delayed skin responses," which many workers are prone to discount. It may signify that the patch test is simply a delayed skin reaction associated with a less intense sensitivity. The difficulty of studying direct skin tests for longer than a few hours is obvious; yet those of us treating allergic patients have seen many instances where, with definitely positive scratch test, reaction by patch test is also striking. One might also conclude from this work that the indiscriminate injection of nonessential antigens (shotgun therapy) is not free from the danger of inducing sensitivity.

Somewhat in contrast with the work of Rackemann and Simon,[21] Brunner[22] found atopic individuals difficult to sensitize by subcutaneous injection of accepted allergens. He did, however, succeed in inducing a sensitivity to orris root, but it was of short duration. Perhaps the subcutaneous injection is not so efficacious as the intracutaneous route since the latter was used by Rackemann.

The peculiar rôle of the skin has been receiving considerable attention in immune as well as allergic phenomena. The study of virus immunity by Donnally and Nicholson[23] stressed the importance of proper skin inoculation. While the difference between allergic and immune processes is granted, it is apparent that inoculation effects will vary with the involvement of the skin per se, which fact is being used in many studies of bacterial products.

The study of nickel dermatitis suggests a link between pharmacologic toxic responses and the response to Rhus extracts. Stewart and Cormia[24] produced a dermatitis in guinea pigs by percutaneous application of nickel salts. The reaction varied with the concentration of the solution (nickel chloride), produced no eosinophilia and was not influenced by preexisting protein sensitivity. Previous intradermal or intraperitoneal treatment made the skin more resistant. They discussed the various interpretations of their experiments.

An interesting and new view of the problem of food allergy was that of Oelgoetz[25] and his coworkers. They suggested that digestion started in the intestine and is completed in the blood stream. An excess of food and a decrease in pancreatic function might cause a relative reduction of the blood enzyme content in the hypersensitive. They proposed a test based on the blood content of free amylase before and after a standard meal. It is difficult to reconcile their hypotheses with earlier experiments in passive transfer[26] in which the allergens, given orally, induced a positive skin test.

CLINICAL STUDIES

The inheritance of an allergic constitution was presented by Bucher and Keeler[27] through five generations of one family, consisting of 236 males and 218 females. With the allergic constitution apparently transmitted as a simple dominant unit character, male and female were affected in equal numbers. Asthma was manifested in 49 per cent, hives or eczema in 42.1 per cent, and there were multiple manifestations in 17.6 per cent of the family.

A discussion by J. F. Smith[28] of clinical aspects of "supersensitiveness" (note the term) convinced the reviewer that many of the British reports are inconsequential. Winnicott's[29] peculiar enthusiasm for a Freudian interpretation of urticaria was likewise not as impressive as some of our own ideas on the psychogenic factors in allergy. More enlightening was Rackemann's[30] review of phases of allergy. This article will be well worth careful reading by those interested in theory based on experience.

The new *American Journal of Digestive Diseases and Nutrition*[31] will apparently be another source of information on food allergy. The first volume contained the Oelgoetz[32] studies and in addition had a timely discussion of food allergy by Vaughan.[33] He gave a general review of the status of food allergy and added a short paragraph on his new leucopenic index test. A preliminary report,[34] devoted exclusively to the leucopenic index, appeared later in the *Journal of Allergy*. Vaughan's first patient had abdominal pains, hives, and headaches following the ingestion of certain foods. In most instances there was an accompanying leucopenia within ninety minutes. He presumed that the ingestion of the offending food produced a mild protein shock which was accompanied by leucopenia as in anaphylaxis. He believed the leucopenic index is a valuable diagnostic adjunct.

Another report on food allergy by Rowe[35] discussed the rationale of the elimination diet. The reviewer has found some of his revised menus and new recipes of great value. There was a general symposium on food allergy by O. H. Brown[36] with his impressions.

The brief for allergic migraine was discussed in the preceding critical review.[37] Opinions expressed by Andresen[38] in his article, "Migraine, An Allergic Phenomenon" in the new Journal, are in direct contrast to those of the reviewer. Andresen held for a definite organic cause of cerebromeningeal edema on an allergic basis. However, when he mentioned desensitization, removal of foci, and the restoration of a "normal endocrine balance," his thesis lost weight. An antidote for Andresen's discussion will be found in an editorial[39] of the *Journal of the American Medical Association*, "The Riddle of Migraine."

During the past year there has been an increased interest and many excellent reports on allergic dermatitis. Williams,[40] in a comprehensive article on cutaneous manifestations of allergy, emphasized the distinction between the allergic and the immune response in the allergic phases of syphilis, tuberculosis, trychophytosis, and bacterial skin diseases. He followed closely Coca's terminology and pointed out the lack of inheritance factors and the necessity of previous contact in the dermatitis.

On the knotty subject of urticaria, the reviewer found the article by Hopkins and Kesten[41] the most clarifying. They divided the external (contact) urticarias into toxic (pharmacologic) and allergic.

The internal causes they listed as serum sickness, food, drugs, inhalants, fungi, bacteria, physical agents, insect bites, metabolic causes, and psychogenic factors. They mentioned the peculiar paradox of negative skin tests in cases in which clinical involvement of the skin was the only allergy. This has been observed by many workers, but few have felt it to be unusual. Could this be related to a lessened state of sensitivity as in Rackemann's experiments in serum sensitivity? The peculiar fixed eruption sites of arsphenamine (drug) urticaria were also mentioned. Hopkins and Kesten successfully treated menstrual (metabolic-endocrine) urticaria by autoserum inoculation. Another interesting citation from their own work was the recovery of a patient with keratoconjunctivitis and adjacent urticaria upon removal of a rabbit hair from the eye. They devoted considerable attention to the rôle of bacteria in foci of infection, especially in the gallbladder. In summarizing the entire subject of urticaria, they concluded that skin tests were usually negative and elimination diets disappointing despite a fair proportion of food allergy in their group of patients.

Mendelsohn[42] likewise discussed this question of sensitization tests and dermatitis and came to similar conclusions. He felt that positive reactions were often misleading as applied to the skin condition and that indiscriminate testing is not justified. He found the patch test of great value when external irritants were involved, but he emphasized the necessity of a proper history and dermatologic survey.

Walzer and Grolnick[43] shed some light on the occurrence of positive skin tests in papular urticaria. They found in such instances that other forms of allergy (atopy) were usually present and that the positive skin tests were referable to the latter and not to the dermatologic condition. They also demonstrated to their own satisfaction that skin tests were of little value in urticaria alone but did not comment on this paradox and dismissed it with the classification "nonatopic."

Here again the orderly mind of Coca[44] has given us a classification. He considered the various types of skin allergy to fall in three groups:

	Technic of Test
1. Atopic dermatoses (familial occurrence)	Intracutaneous Scratch or indirect
2. Contact dermatitis (nonfamilial)	Surface contact or patch test
3. Fungous dermatitis (eczematous dermatophytids)	Intracutaneous or patch

The reviewer is glad Coca coined no new terms since much of the recent work has tended to discard some of his earlier classifications.

It was only a year ago that Sulzberger and his associates,[45] who follow Coca's terminology rather closely, claimed that silk sensitivity was often accompanied by a positive cutaneous test but its significance in dermatoses was open to question. This year he and Vaughan[46] reported a study of positive skin tests to silk with negative patch tests and claimed that the dermatitis resulted from inhalation of silk. While obviously not a true "contact dermatitis," this finding showed the danger of too early a pronouncement regarding phenomena and their classification.

Coca,[47] discussing allergic skin diseases, was encouraged by the reports of improvement in atopic conditions following surgical eradication of purulent infection. The rôle of infection in precipitating or aggravating "atopic" responses, does not seem new, and the implications of Burky's[48] work, previously cited, are of definite importance. The reviewer has witnessed the swing from the radical program of surgical removal of tonsils and adenoids and antrum irrigations to the equally extreme refusal to allow removal of obviously infected tonsils because the patient was allergic. Perhaps we are now ready for the middle of the road. In any event, the study of bacterial toxin influences may be as important as the rather vain search for criteria of the "allergic constitution."

Coca mentioned the newer work of Sulzberger on silk sensitivity, though the reviewer would point out that this was first described by Figley and Parkhurst[49] and Taub and Zakon[50] at a time when Sulzberger[51] considered silk dermatitis as only a contact response.

More justifiable is Coca's[52] enthusiasm regarding Sulzberger's[53] work on the rôle of fungi in dermatitis. The latter showed skin test phenomena differentiating monilia and trychophyton infection and paved the way for therapeutic hyposensitization. Templeton[54] and others have already verified its clinical application.

Hill's[55] work on infantile eczema, however, is inconclusive. He found 15 per cent positive reactions to *Monilia albicans* in a group of patients with eczema and 8 per cent positive reactions in a control group. When the difficulties in testing young infants are considered, his results are not surprising.

Straus[56] has continued his researches on dermatitis venenata. In his earlier reports[57] there was the suggestion that sensitivity could be established by oral administration of Rhus extract. His 1934 reports showed that oral administration is not sufficient and that the contact or dermal route is essential. Spain, Newell, and Meeker[58] have also studied susceptibility to alcoholic extracts of Rhus. They found no apparent effect from first applications of the extracts.

White[59] found the ordinary skin tests of little value on acneform dermatitis; yet food allergens were definitely responsible. Nonallergic trial diets were diagnostic and therapeutic. Ragweed dermatitis was studied by Brunsting and Anderson,[60] who found that the irritant was not limited to the oil fraction of the pollen (Coca) and that the almond-oil extract treatment of Gowen[61] was difficult to evaluate. The reviewer feels, however, that in general this treatment of many of the similar dermatoses is very helpful. A case of cedar bark sensitivity was apparently benefited by the oil-cedar-extract treatment. Rowe[62] reported the occurrence of camomile as a skin irritant resembling Rhus. Previous contact was apparently a factor, and its widespread occurrence added to its importance. The dermatitis attributed to socks was found by Schwartz[63] to be the action of the dye or the "finish," and washing removed or altered the irritating fractions.

Peculiar forms of light sensitivity were presented by Anderson and Ayers.[64] They discussed hydroa, vitiligo, and lupus erythematosus, the rôle of dyes, drugs, foods, and infections as sensitizing adjuncts and those little understood factors of sulphur metabolism and the significance of prophyrin.

"Another case" of urticaria by cold was reported by Dubbs.[65] He was apparently able to control the symptoms by calcium administration but hoped to try hyposensitization by graded exposure or histamine injection in order to obtain more permanent improvement. The danger of allergic reactions, following transfusion, was illustrated by the response described by Tedstrom.[66] Far too frequently transfusions are given regardless of the possible factors of allergy.

A discussion of insulin allergy by Davidson[67] showed that even the most purified insulin is of an antigenic nature. He found sensitization was rare and the relation of this allergy to diabetes, merely casual.

Spain and Newell[68] were able to show the presence of reagins in blister fluid by producing blisters with cantharides. A number of passive transfers to a variety of inhalants were obtained.

Carey and Gay[69] reported on skin tests in infants. They found a variable reaction to histamine but no difficulty in obtaining passive transfer. They referred to Bell's[70] work but failed to mention the earlier work of Smyth and Bain.[71]

R. A. Cooke's[72] article on asthma in children is, as usual, well worth reading. His paper covered causes, diagnosis, and treatment. He also discussed immediate as opposed to delayed clinical symptoms, but at the same time he felt that delayed skin tests were of no significance. The rôle of familial incidence, intrauterine contact (placental transmission of Ratner), specific and nonspecific excitants were also discussed. He considered the pulmonary response in asthma one of edema rather than bronchospasm and felt that infective agents may act as foci long after the acute stage. The usual finding of food allergens in infants and inhalant allergens in older children was borne out in his experience. The reviewer was surprised at his recommending morphine for children during acute asthmatic attacks and the injection of food antigens rather than their avoidance. Likewise surprising was his endorsement of x-ray treatment rather than tonsillectomy for tonsillar infective foci. He stressed general measures and the anticipation of allergy in the young of allergic families.

Duke[73] reported soy bean as an excitant of allergy and discussed its action either as an inhalant or food allergen, its distribution, and uses. His report is of interest in cases in which Sobee is a substitute for milk for allergic infants.

The standardization of pollen extracts has continued to be a much argued point. Coca[74] suggested that the Noon pollen unit be revised as 0.00001 mg. of total nitrogen. Spain and Newell[75] studied the effect of ultrafiltration of ragweed pollen which separates protein nitrogen and nonprotein nitrogen fractions. They concluded that the phosphotungstic acid precipitable nitrogen (standardization method of Cooke and Stull) did not correspond exactly with the allergic activity but was still the most practical method. On the other hand, Bowman[76] found by biologic assay (skin test) that the standard of Cooke and Stull was fallacious. The reviewer feels that too fine a standardization may not be warranted at the present time and either standard is practical.

Moore and Unger[77] concluded that the pollen allergen must be of a protein nature because of its susceptibility to enzyme digestion.

Pollen surveys were made by Barrett,[78] working in the Utah region, by La Rush[79] in Toronto (1932), and by Lamson and Watry[80] in northern Arizona.

Dushan and Cohen[81] proposed a puncture method for skin tests which they found superior to the usual type of abrasion. In studying pulmonary and dermal tests of sensitivity to inhalants, Stevens[82] found no greater reliability in the former than in the latter. They were unable to confirm any local specificity of tests by the use of spray applications and concluded that the test-negative group remained about 50 per cent of the total. Rudolph and Cohen,[83] however, in their report on vasomotor rhinitis with negative skin tests found a local nasal test helpful. Their application was by pledget which suggests a mucous membrane test comparable with the local patch test for dermatosis. They considered the condition a local allergy. If their test is a delayed response, the reviewer wonders if patch test to the skin might be positive or if they would suggest an oil-extract hyposensitization, such as has been advocated for "contact dermatitis." It would also appear difficult to control nonspecific effects in their "pledget" tests, Somewhat parallel was the suggestion of Forman[84] that while vasomotor rhinitis is as a rule "atopic," there are a few instances where skin tests are negative and a contact "coryza" exists. He had a diagram for aid in studying these nonreactors. The conjunctival test was found less sensitive than the skin test by Simon.[85] His case report seemed most unusual. The patient had vasomotor symptoms and was sensitive not only to horse serums but also to all mammalian serums. Passive transfer was obtained. He thought his case illustrated a common denominator in the various serums. If such conditions are more prevalent than is commonly supposed, reactions from the antitoxins from sources other than the horse can be explained. In reference to horse dander and horse serum sensitivity, he considered the condition acquired. He found certain horse-sensitive asthmatics might tolerate antitoxin. He advised conjunctival as well as skin tests before administration of therapeutic serum.

In the field of treatment, Brown[86] continued his enthusiasm for massive pollen therapy. He did not consider the method to be particularly dangerous although some of us dealing with children would hesitate to adopt such a program for general use. In this respect the report of Lichtenstein[87] on the use of intravenous pollen therapy was startling to say the least. He did not think the method dangerous and found a resultant definite depression of the skin test though the blood contained ample circulating reagin. Considering the usual caution which the reviewer has felt necessary for pollen injections and the occasional severe reaction in spite of precautions, he wonders if Lichtenstein has yet to encounter episodes likely to modify his present opinion.

Waldbott and Ascher[88] have also studied rapid hyposensitization with the conclusion that the method is not without danger but can be used in certain urgent conditions. Moore and Unger[89] compared dextrose pollen extracts with those in a glycerin vehicle. Results in treatment were similar, but dextrose solutions were less painful and easier to handle. The reviewer wished for more comment on the relative sterility of the two solutions. Unger and Moore[90] believed that perennial was better than preseasonal treatment. Walker,[91] on the contrary, felt that preseasonal treatment of hay fever with proper pollen ex-

tracts, offered permanent relief. As a rule, however, three to six courses of such treatments were necessary, and in such instances an average of 75 per cent of those treated were relieved.

Rappaport and his coworkers[92] considered viosterol of definite value when used with the specific treatment of hay fever and that the latter alone was not so efficacious. They suggested, not a calcium effect per se, but a potassium-calcium ratio control. Rappaport has been persistent in his advocacy of viosterol. It is a matter of conjecture what undesirable effects might be obtained by continuous use of very concentrated vitamin D.

Some peculiar phenomena of allergic nature have been reported during the past year. Massy and Gilmore[93] described a violent reaction to the Schick test given for the third time. Toxoid had been used previously, and the serum titer showed immunity to diphtheria. The instance was obviously one of sensitization. Cole and Korns[94] described visceral manifestations of angioneurotic edema and considered the pulmonary symptoms Quincke's edema of the lungs. Waldbott[95] discussed shock reactions from substances other than pollens and serums. He likewise attibuted the reactions to a sudden edema in various parts of the body. These reports of Walbott on allergic death should check any enthusiasm for procedures such as have been already discussed with reference to Lichtenstein's intravenous pollen therapy. With Ascher, Waldbott[96] reported a neuropsychiatric reaction which simulated these allergic shock conditions and pointed out the difficulty in differentiating "asthma nervosa."

Harkavy[97] has continued his observations on tobacco sensitivity in relation to thromboangiitis obliterans. In normal smokers he found parallel reactions between tobacco leaf and pollen, i.e., allergy with multiple sensitivity. In patients with thromboangiitis obliterans, reactions to leaf alone were characteristic. With Romanoff,[98] he substantiated his earlier claims[99] by reporting 69 per cent positive reactions to tobacco in patients with thromboangiitis obliterans, while only 11 per cent were positive in the control group. Suggestive of Vaughan's leucopenic index in food allergy is the report of Squier and Madison[100] of primary granulocytopenia due to hypersensitivity to amidopyrine. It will be interesting if this cytologic finding proves characteristic of many ingestant allergies. Frumess'[101] report on allergic reactions to dinitrophenol added a new drug to the list of potential allergies and suggested the need for caution with regard to its use.

A further study of Caddis fly allergens by Osgood[102] pointed to the existence of one factor common to both species of the fly, while an additional allergen was confined to one of the species. Fisher and Center[103] reported successful treatment of "bee" sensitivity with whole bee extract. This, of course, is a further verification of Benson's[104] work previously discussed. Considering the occasional instances of sensitivity to that well-known insect of San Francisco, the reviewer takes courage to apply this treatment for flea sensitivity. Those who rely on the use of pyrethrum insecticides for such conditions will find the comprehensive discussion on pyrethrum sensitization by Fineberg[105] most helpful. From his own observations, the reviewer can speak with feeling on Eastern visitors who, sensitive to ragweed, attempt to use substances containing pyrethrum to combat the San

Francisco flea. The result is not unlike the proverbial jump from the frying pan into the fire. Taub[106] has likewise given a rather full report of the widespread uses of cottonseed. Found as an ingestant, contactant, and inhalant, cottonseed assumes a rôle of major importance in those sensitive to the substance.

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American Academy of Pediatrics

JOHN RUHRÄH

1872-1935

JOHN RUHRÄH, of Baltimore, Md., a widely known and much beloved pediatrician, died at Mercy Hospital, Baltimore, March 10, 1935. He was born September 26, 1872, in Chillicothe, Ohio.

In October, 1930, after attending the International Pediatric Congress at Stockholm, he suffered an attack of poliomyelitis from which, after a long siege of illness, he recovered sufficiently to enable him to resume his practice, also to travel, and to engage in many of his lifelong activities, though a residual paralysis of his lower extremities persisted. About two months ago, while examining a patient in his office, he was suddenly attacked with what appeared to be an apoplectic seizure. He was removed to Mercy Hospital on January 17, 1935. His mind was clear almost to the last, and during his final illness he retained that fine humor and stoicism which had characterized his whole life.

Ruhräh was graduated from the Chillicothe High School in 1891 and received his medical degree from the College of Physicians and Surgeons, Baltimore, 1894. He took postgraduate courses at Johns Hopkins Hospital Medical School, at l'Institut Pasteur in Paris, 1897, and at the universities and hospitals of Vienna, Berlin, and Paris, 1900, 1901. He was assistant resident physician at Mercy Hospital, 1894, 1895, and resident physician, 1895-1897. He was physician in charge of the Pasteur Department of the College of Physicians and Surgeons, 1897. From 1898 to 1900 he was quarantine physician at the port of Baltimore. At about this time he was appointed to the chair of diseases of children at the University of Maryland Medical School, a position which he held for many years. He was also visiting physician to the Mercy Hospital, consulting physician to the Church Home and Infirmary, and visiting physician to the Hospital for Women of Maryland.

He was elected president of the Medical and Chirurgical Faculty of Maryland in 1919, President of the American Pediatric Society in 1912, president of the Medical Library Association in 1927, president of the Research Society in 1932, president of the Osler Historical Society in 1933, and president of the American Academy of Pediatrics in 1934. He was a member of the Board of Education of Baltimore. In 1932 he was selected by the Baltimore City Medical Society to prepare a history of the medical profession in Maryland for the last quarter of a century, a task which he was well qualified to perform. He entered private practice in Baltimore in 1901 though he continued his academic connections, teaching bacteriology, pathology, and clinical medicine in the College of Physicians and Surgeons. He never married.

He was a facile writer. His style was terse, with occasional shafts of fine humor, and his wide reading in many languages manifested itself in his numerous pertinent references from many fields of literature. Among his books may be mentioned: *Diet in Health and Disease* (with Julius Friedenwald), sixth edition, 1925; *Dietetics for Nurses* (also with Friedenwald), fifth edition, 1924; *Manual of Pediatrics of the Past*, 1925; *Pediatric Biographies*, 1932; *William Cadogan, His Essay on Gout*, 1925; *Poliomyelitis in All Its Aspects* (with E. E. Meyer),

1917. He contributed articles on pediatric subjects to most of the modern American encylopedias and systems of medicine, among which may be mentioned: Osler's *Modern Medicine,* Nelson's *Living Medicine,* Tice's *Practice of Medicine,* and Abt's *Pediatrics.* Ruhräh made the first collective investigation of actinomycosis in the United States, 1899-1900, and he introduced the soy bean in infant dietetics, 1909.

One of his impelling interests was his love of books, which showed itself in his passion for the study of "the old worthies" in the pediatric literature. During the past several years he has been a regular contributor to the *American Journal of Diseases of Children* on the subjects of pediatric biographies and pediatrics in art. His biographic sketches refer to interesting pediatric writers of the past, and his art

sketches, to reproductions of interesting illustrations of various phases of child health and hygiene. He sometimes was given to writing verse, and at medical meetings he would become inspired to write a few stanzas suggested by the themes under discussion, in which he would humorously reduce the highly involved scientific presentations to common-sense interpretations. His poem on infant feeding became famous.

Ruhräh had a matchless personality and a great facility for establishing enduring friendships. He had a charm and graciousness of manner which led one to feel at home in his presence. He was extremely tolerant. He forgave shortcomings and appreciated even the minor virtues of his fellow men. He mingled well with all classes of people. The lowly and untutored did not repel him, and he met the intelligentsia gracefully and with exceptional poise. He was a brilliant conversa-

tionalist, scintillating and entertaining. He was always reminded of a choice tale from a rare book or a forgotten author. It was a treat to enjoy his companionship during a leisure hour.

His artistic tastes were not confined only to art and literature. He was also a devotee of fine music. It was said of him in Baltimore that he scarcely ever missed a worth-while musical event at the Lyric Theater. He made the annual pilgrimage to Bethlehem, Pennsylvania, for the Bach music festival, which he spoke of to his friends as one of the most important events of his year. On his numerous trips to Europe he made it a point to visit one or more of the summer music festivals.

Ruhräh lived a full life. He combined the activities of the practitioner of medicine with a large degree of human understanding and common sense. He had an artistic nature which craved the cultural things in life. These he found it possible to provide for himself. After his severe affliction, by undaunted courage and indomitable will, he was happily able to resume his work and his recreations. He gradually took on new tasks and carried on with joy and zest until the final illness. John Ruhräh leaves a rich heritage of devoted service dedicated to medicine and humanity.

"A man beloved, a man elect of men."

—Swinburne.

I. A. A.

Proceedings

FOURTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

JUNE 11, 12, 1934

Round Table Discussion on Disorders of the Blood

Leader: Dr. Thomas B. Cooley, Detroit, Mich.

CHAIRMAN COOLEY.—It is my purpose to bring up for discussion today some points regarding the genesis and therapeutics of anemia, prefacing this with a few remarks on the structure of the red cell.

We know really surprisingly little about the make-up of this highly important cell. Even the traditional beginning of all descriptions of it, that it is a biconcave disk, has been questioned, and it has been likened rather to a saucer, or a rubber ball with the air squeezed out. The familiar conception is of a limiting membrane of some sort, enclosing a stroma, in which the hemoglobin is deposited. This stroma has been thought of as a spongy mass, or as a sol or gel, which might ooze out if the cell were damaged, while it has been assumed that the limiting membrane is chiefly protein. Though analyses are somewhat uncertain because of difficulties in removing all the hemoglobin, such analyses as we have indicate that there is not enough protein in the cell structure to form a membrane more than two molecules in thickness. It is known that a considerable part of the cell is composed of lipids, formerly supposed to be chiefly cholesterin and lecithin, though now cephalin is believed to be present in important amounts. It is probable that these lipids form a part of the membrane. They may be deposited in the interstices of a loose protein network or may form a layer either on the outside or the inside of the protein framework. The lipid mixture seems to have colloid properties which would vary if the relative proportions of the lipids were altered, and it has been suggested that something of this kind might account for changes in the permeability of the membrane. Certainly, the cell's lipid content may be supposed to have a good deal to do with the types of hemolysis due to fat solvents. It is by no means certain that the hemoglobin is contained in the interior of the cell, and there are some good reasons for thinking that it may be deposited in the membrane, perhaps in the lipid layer, in which case the interior of the adult cell, after the loss of the nucleus, would contain only fluid derived by osmosis from the plasma.

Whatever one's conception of the physicochemical structure of the cell may be, it seems evident that the cell structure must vary considerably under certain disease conditions. The remarkable changes in shape which the cells undergo in sickle-cell anemia, for instance, must depend on abnormalities of structure, and it is easy to believe that the excessive destruction of the cells in some other anemic states is a result of structural defects or peculiarities.

THE GENESIS OF ANEMIA

Anemia is a condition in which the proportion of hemoglobin in a given volume of blood is less than normal. This hemoglobin deficit may or may not be accom-

panied by a lowering of the red cell count; on the other hand, if the cell count is markedly lowered, there will of necessity be a hemoglobin lack also.

Whatever the fundamental cause of the state may be, the actual production of anemia can be only by some one of the following:

1. Direct blood loss
2. Failure of red cell production or maturation
3. Excessive cell destruction
4. Failure of hemoglobin formation
5. Combination of two or more of the above factors.

Direct Blood Loss.—The mechanism of anemia production from this cause needs no special comment.

Failure of Cell Production.—A. Marrow Hypoplasia: By this we mean a condition in which the erythropoietic activity of the marrow is for the time being partly or wholly suspended. Capacity for function remains, however; and when the cause of the hypoplasia is removed, normal function returns.

Such a state seems to be an important factor in many of the secondary anemias, especially those arising in the course of infections, in which it may be supposed that the toxins of the infections have a depressant effect on the marrow. It may be assumed to occur in conditions of under- or malnutrition, in which the general metabolism is below par, or in which special metabolites which stimulate hemopoiesis are lacking. It is apparently a factor in some of the anemias, precise etiology and pathogenesis of which are little understood.

B. Aplastic States: Marrow aplasia may be said to be a condition in which so much of the active marrow is atrophied or destroyed that cells sufficient for the body's needs can no longer be produced. Poisoning by arsphenamine, benzol, etc., may have such an effect, as may physical agents, such as x-ray and radium. Certain infections may have it as a sequel. Prolonged hypoplasia may finally result in marrow atrophy. In certain, probably constitutionally susceptible, individuals the anemia of hemorrhage may be followed by aplasia. Prolonged sepsis is one of its rather common causes. The type of aplasia which results from infiltration of the marrow by pathologic tissue, as in leucemia and malignant disease, is often spoken of as "myelophthisis."

Aplasia affects both erythropoietic and leucopoietic tissue and is characterized by progressive disappearance of all types of marrow cells from the circulation, without signs of regeneration.

C. Lack of Structural Material: The idea that in certain conditions red cell production is interfered with because the marrow is not being furnished with material necessary for the construction and normal development of the cell body is, in the present state of knowledge, largely a matter of inference from the effect of certain therapeutic procedures. From what has been said of our meager knowledge of the cell structure, it is evident that this must be a difficult thing to prove; but the fact that the erythrocytes in some diseases have an obviously abnormal structure argues for the probability.

Abnormal Destruction.—Excessive erythrocyte destruction is an important feature of many of the anemic states. In the "primary" constitutional hemolytic disorders the marrow apparently produces cells of defective structure, which are more readily affected by the destructive processes than is the normal cell.

Infectious states often produce a picture of increased destruction, usually by an exaggeration of the normal process of fragmentation. As hypoplasia is also common with infection, these two processes may be found combined. In such case the destruction usually ceases with the infection, while the hypoplasia may persist for some time after. The reason for the increased fragmentation is not clear. The toxins of infection might be supposed to act upon the marrow to cause it to pro-

duce defective cells which break down easily, or they might act upon the formed cells to make them more fragile. As compared with this process of fragmentation, such hemolysis as goes on in hemolytic icterus under the influence of the spleen probably has little importance in the ordinary secondary anemias, nor is extensive phagocytosis of whole red cells a common phenomenon, though it is possibly of importance in some of the constitutional anemias.

Failure of Hemoglobin Formation.—Iron is not the only important constituent of the hemoglobin molecule. The pigment radicle, with its pyrrhol nucleus, and the amino acids which go to make up the globin fraction must be taken into consideration also. It is only recently that it seems to have been shown that the body is capable of synthesizing the pyrrhol nucleus, which it had previously been supposed we must get from outside. These constituents other than iron have received a good deal of attention in recent years, and, while we must still believe that iron is the chief factor to be considered in defective hemoglobin synthesis, the success of therapeutic methods aimed at supplying other "building stones" indicates clearly that in many cases it is not the sole or indeed the chief lacking ingredient. Some of the substances, such as copper and the vitamins C and G, which are believed to be important to hemoglobin synthesis, do not actually enter into the hemoglobin molecule, but must act in some way not perfectly obvious to determine the reaction.

Combinations of Two or More Factors.—These are common; in fact, there are probably few anemic states in which any one of the factors mentioned is solely responsible.

Hypoplasia and increased destruction are often associated in the anemias due to infection.

Recurrent bleeding may result in aplasia, while the aplastic state commonly causes hemorrhage.

Long-continued bleeding may so deplete the body's store of blood-building materials as to cause a "deficiency anemia," in which more than one of the essential building stones may be lacking.

The purest type of anemia should be the form of "nutritional anemia" due to depleted iron reserve, but even here infection sooner or later is likely to complicate the picture by introducing a hypoplastic or a hemolytic element.

THERAPEUTICS

Our therapeutic efforts must of course be based, in the given case, on our conception of the pathogenesis and on the ability of the various items in our armamentarium to meet the apparent indications. For our present purpose the best method of approach to this question is probably to consider individually the various procedures in vogue and what we know of their applicability in the different anemic states.

The Uses of Iron.—There is no question that iron still holds first place among the antianemic medicaments, and for more than one good reason. In many anemias, particularly those of premature infants and twins, there is good reason to think of a probable exhaustion of the stored iron, which by all evidence can be more rapidly replaced by oral administration of suitable iron salts than by feeding of iron-containing foods. In all of the hemolytic anemias there is more than the normal loss of iron from the body, and there is also a need for a resynthesis of hemoglobin to replace that destroyed. While the iron of the destroyed cells is probably largely used over again, we have no definite evidence as to the rapidity with which this process of reutilization goes on; and it seems only common sense to be sure that the hemopoietic tissues are assured of a proper supply of this important part of the hemo-

globin molecule. Theoretically, the only anemic processes in which iron could be said not to be indicated would be those (hypoplasia and aplasia) in which the marrow is unable to utilize it. There was a very general loss of faith in the efficacy of iron until the present tendency to give very large doses, since when it seems to have come into its own again. More than one reason is suggested for the efficiency of these large doses, many times greater than any possible need for hemoglobin synthesis. A time-honored one is failure of absorption, a reason which certainly has some force. Whipple believes in a possible "salt action," as to the nature of which he is not very clear. A recent idea is founded on the experiments with copper. Practically all of the iron used contains minute amounts of this metal, and it is not impossible that the very large doses of iron are effective because they are the means of administering copper in sufficient amounts.

Some recent work has been done on the availability of different iron compounds. It seems to be quite generally agreed that the organic preparations are the least useful and that the best are the inorganic salts already in solution, or readily dissolved by the HCl of the stomach. The Wisconsin workers found the pyrophosphate especially good. Parsons cites some trials supporting Heubner's contention that the ferrous salts are better than the ferric compounds. In this country iron and ammonium citrate and, for children, the saccharated carbonate are favorites.

Parenteral injection of iron, by one route or another, has had considerable vogue. It has the apparent advantage that one need not reckon with uncertainty of absorption, but we have been unable to see that it has anything else to recommend it, as it is neither more reliable nor more rapid in its effect.

Copper.—The demonstration by the Wisconsin group that the addition of small amounts of copper to iron preparations is of great value in treating anemias of experimental animals has aroused much comment. Some competent hematologists are not convinced that these findings are applicable to humans, but the tendency to add copper seems to be spreading. In our own experience we have thought that the addition of copper enabled us to get results with smaller doses of iron, though this is not always true, and we not uncommonly find that we achieve this same effect more readily with liver, even in what seem to be simple iron deficiency anemias.

Inasmuch as copper is not a component of the hemoglobin molecule, it is assumed that its rôle is that of a catalyst.

Liver.—The use of liver, in the form either of the cooked meat, or of extract of whole liver, has grown greatly in the last few years, thanks largely to the work of Whipple; there can be no doubt now of its value. The special extract used in the treatment of pernicious anemia is of little service in the ordinary anemias, and, according to some investigators, there are conditions in which the cooked flesh is more effective than any extract.

Liver seems to have its chief value in those types of anemia in which there is need for new cell building, rather than in those in which there is simply a hemoglobin deficit, though there are indications that at times it furnishes something needed for hemoglobin synthesis. There are many evidences that the liver is both factory and storehouse for materials of blood building. It is the source of several of the factors in the clotting mechanism; it is the infant's storehouse for iron and copper and the principal place of deposit also for the pigments resulting from blood destruction; it is a fair deduction from its observed therapeutic effects that the liver furnishes other still unidentified substances that go to red cell building and development. One of Whipple's experiments, in which he fed to his dogs the livers of patients who had died in various anemic states, showed that in some of them there had been a tremendous storage of blood "building stones," presumably because the marrow in these diseases had been unable to use them. Whipple has been able to show that iron and liver often have a remarkable complementary action, such that

the effect of the two given together may be more than the sum of their individual effects. It is rather a common observation, when both cell count and hemoglobin are low, that the giving of liver alone causes an increase in the cells while the hemoglobin lags until iron is added. Sometimes, if iron alone is given first, precisely the same sequence is observed, with the liver giving the final stimulus to hemoglobin deposition. This is not so easy to explain. The idea, quite generally accepted for the effect of liver in pernicious anemia, that it furnishes a "maturation factor," can hardly be applicable in all of the types of secondary anemia in which it is found effective.

Marrow Extract.—Theoretically, the red marrow should contain practically everything that goes to the building of the cells, and an active extract should be a useful addition to antianemic preparations. We have made considerable trial of one extract, and, while we have at times thought that we were getting some benefit from it, our results were not wholly convincing. Whether a different preparation or larger doses might work better, we cannot say. We have also tried the extract of yellow marrow, used in some clinics for a supposed stimulus to white cell formation, with no perceptible effect.

Splenic Extract.—This has the weight of Krumbhaar's recommendation, its use being based on a supposed regulatory of splenic products on the marrow. We have had little experience with it. It is a constituent of some proprietary preparations.

Amino Acids.—Since the globin portion of the hemoglobin molecule and the protein framework of the cell must depend on essential amino acids for their synthesis, it is natural that trial should have been made of some of these substances in therapeutics. Injections of histidine, arginine, glutamic acid, and tryptophane have been used, and some good results have been reported. These reports are not wholly convincing. But since the work is still in the experimental stage, it is not at all improbable that something definite may come of it.

Vitamins.—There are no characteristic anemias recognized as due to vitamin lack. There is evidence that vitamins C and G are essential to normal blood building, but even scurvy does not always cause definite anemia. It would seem probable, however, that the disturbed metabolism accompanying any vitamin lack might well result in a secondary hypoplastic anemia, and it would be only common sense to correct any such deficiency. Occasional anemias are cured with no further treatment than this.

Diet and Hygiene.—It is generally recognized that the "iron deficiency" anemia due to exhaustion of the iron reserve can usually be prevented, and sometimes cured, by timely introduction of iron-containing food in the diet. This is a precaution to be taken particularly with premature infants and twins; when such an anemia has developed, it is, of course, important. Information as to other specific dietary needs is not so clear. Liver is commonly included in antianemic diets and sometimes seems more effective given in this way than as an extract. Kidney, according to Whipple, is nearly as good. Red meat ranks high in the list of blood-building foods. Eggs have always been rated high. Some of the vegetables long touted for their iron content, such as spinach, have not been proved to have special value, while peaches and apricots are given high rank. On the whole, the requirements of an antianemic diet, so far as we know them now, are that it should be as liberal and varied as the patient's age permits and should contain a generous proportion of the things known to favor blood building. The idea once prevalent that milk tends to produce anemia and should be excluded has disappeared. Its effect is bad only when it is used too long to the exclusion of other foods.

The need of sunshine and fresh air is not to be forgotten. One meets occasionally with mild hypochromic anemias which in our northern winter climate are refractory to all medicinal treatment, but which are cured promptly by transfer to the South.

Transfusion.—A long list might be compiled of the conditions in which transfusion is supposed to be helpful. So far as the anemic states are concerned its most definite effect is the rapid replacement of cells, and, in the anemia of hemorrhage, of plasma constituents as well. It seems probable that besides furnishing cells to carry on normal oxygen metabolism, it also, by raising the general metabolism level, helps the marrow to function better, and thus may be looked upon as a stimulus to hemopoiesis. It must furnish some blood-building material which may be needed. As the most reliable method for checking bleeding when the clotting mechanism is at fault, it is a preventive of increasing anemia in these conditions.

It is often a question when a given patient is in need of transfusion. It is true, in general, that the patient whose hemoglobin has fallen rapidly does less well at the same hemoglobin level than one with a more chronic type of anemia, who has gradually become accustomed to it. Thus one whose hemoglobin has fallen rapidly to 6 or 7 gm. may be in more urgent need of transfusion than one in whom it has declined gradually to 4 gm. While it is difficult to say, except in case of severe hemorrhage, just when a transfusion is necessary to recovery, it is often obvious that timely transfusion will greatly hasten the process, and it is usually wise, in grave anemias, to inaugurate treatment in this way rather than to wait for the effects of medicinal measures, which will be useful when transfusion has put the patient in better position to take advantage of them.

There has been some difference of opinion as to the duration of life of the transfused cells. We were able to study this over a long period in one case and to satisfy ourselves that the average life of the cell after transfusion was from two to three weeks. This does not, of course, mean that the total life of the cell is not considerably more than this.

There is no question that the intravenous method of transfusion is the most satisfactory. Intraperitoneal injection has a slower, less sure effect but is useful for repeated doses when there are obstacles to the intravenous technic. The discussion over relative merits of citrated and noncitrated blood is of little importance. Theoretically the noncitrated blood is better when the platelets are needed.

Intramuscular injection of blood does not furnish red cells to the circulation. Blood given this way does furnish plasma constituents, which may be utilized by the marrow, and products of cell disintegration, which by a chemotactic effect may be stimulant to hemopoiesis.

Josephs has recently shown that in certain of the hemolytic anemias the injection of concentrated plasma has an effect closely paralleling that of transfusion in the same disorders. This must be due to its furnishing some essential building stones for which it is the normal carrier.

Splenectomy.—The vogue of splenectomy is growing steadily. It is being tried now in a wide variety of conditions, in some of which the indications are rather vague, and the results are not yet convincing. We are concerned here only with what may be expected of it in anemic states. Its chief indication seems to be to put a stop to a pernicious activity of the spleen, which is most readily denominated, in the lack of a complete understanding of its nature, as "hypersplenism." Since this condition lies at the bottom of the type of hemolysis met with in hemolytic icterus and apparently in erythroblastosis of the newborn, removal of the spleen almost invariably puts an end to it, as this particular splenic activity seems not to be readily taken over by other depots of reticuloendothelium.

The two conditions in which it has scored its most marked successes are hemolytic icterus and hemorrhagic purpura, in both of which it may be said to be almost a certain cure; its success in these diseases is an important point in the reasoning as to their pathogenesis.

There are no other anemic states in which its results are so striking. It has been practiced in many, perhaps most, of the recognized cases of erythroblastic

anemia, merely to rid the patient of the burden of the greatly enlarged spleen. It does not appreciably affect the disease process, though possibly the patients live somewhat longer than they would otherwise. In sickle-cell anemia we have found that we can mitigate the abdominal crises, and perhaps the joint symptoms, by the operation, but the anemia is little changed. It is generally believed that in "splenic anemia" early splenectomy lessens the probability of development of hemorrhage and cirrhosis, which are the later stages of the Banti syndrome. Unfortunately, this effect cannot be definitely depended upon. If one accepts the idea that the spleen normally exerts a control over marrow activity which may be perverted in some states, there might be an argument for splenectomy in obstinate hypoplasia which threatens to go on to aplasia.

One is often questioned as to possible deleterious effects of the operation. It is really remarkable that so important an organ can be removed with so little apparent effect upon the general body economy. The explanation must lie in the readiness with which the rest of the reticuloendothelium takes over the splenic functions. Just how serious the loss of the splenic reservoir might be in time of stress can hardly be estimated.

It has been generally accepted that it is dangerous to remove the spleen during a hemoclastic crisis, and in most clinics, certainly, it is the custom to endeavor to carry the patient over the crisis and operate at a more favorable time. Since emergencies will arise, however, in which operation seems imperative, with the improvements which have come in technic, the results of these emergency operations may prove less discouraging.

Some Practical Points.—The management of the ordinary case of secondary anemia is a matter of good hygiene, proper diet, and a selection of pharmaceuticals to meet the indications. One must always remember, however, that in the commonest form of anemia, that due to infection, medicinal treatment is notoriously ineffective as long as the infection persists. If the condition is serious, frequent small transfusions may be needed, both to counteract the anemia and to help the patient to throw off the infection and break the vicious circle.

As to pharmaceuticals—in the clinic it is of interest to experiment with various combinations of iron, liver, copper, etc. The private practitioner, whose main purpose is to achieve prompt results, will usually do better with some one of the "shotgun" preparations which are now met with in abundance. The most important ingredients to be looked for are iron and liver extract. We use for routine treatment a combination of iron, copper, and liver and marrow extracts, which in varying dosage answers practically all our requirements. None of the liver extracts are especially palatable, and it may require some ingenuity to get the child to take them. For older children, they may be had in capsules.

There is at present a great deal of discussion as to the desirability of adding iron to the food of all young infants—based largely on the work of Dr. Helen MacKay. We are not yet convinced of the need of this with children of good stock, living in favorable surroundings, and the present evidence is that with premature infants and twins, in whom early anemia is especially likely to develop, neither iron nor liver can be depended on to forestall this.

DISCUSSION

DR. ARTHUR ABT (CHICAGO).—I have enjoyed Dr. Cooley's presentation immensely. His etiologic or causative classification reminded me of Czerny's classification of the nutritional diseases. It is the most difficult classification to make because there are so many mixed types. Personally, I am not so brave. If I have a case of anemia during or following infection, I put it in the clinical group of infectious anemias. If the infection prevents the child from taking proper diet, or

perhaps from assimilating the diet, we call that the "alimentary-infectious type." When the clinical basis for the anemia is simply an improper or unbalanced diet, I should call it an "alimentary anemia."

Dr. Cooley has made us realize how little we really know of the physiology of the red cell, when even so simple a thing as its shape has been in doubt.

The resistance of the red cell is an interesting thing. I think Goldbloom, of Montreal, showed that the resistance in the newborn infant is less than that of the older child. We know very little about the mechanism of this greater or less resistance. Dr. Cooley's idea that it may have to do with the lipid structure was new to me.

Some have thought that the infant during the first year may have a different kind of hemoglobin than the older child. Horwitz found a difference spectroscopically between the blood of infants and that of older children.

DR. COOLEY.—I was not trying to classify the clinical types of anemia, but the factors in pathogenesis, quite a different matter. We classify our anemias clinically much as you do.

I might say a word further as to the possible relation of the lipids to resistance. It is rather striking that the most active hemolytic agents we have are things, such as saponin and ether, which would be more likely to affect the lipid than any other part of the cell. Bechhold, as far as I know, was the first to suggest the probability of variations in the absolute and relative proportions of the different lipids in the cell and their possible relation to the cell's permeability. There are not as yet any good analyses of the lipids in pathologic states.

DR. COOLEY (In reply to several questions).—The makers of a rather well-known proprietary preparation have been furnishing us with the separate ingredients in the menstruum which they use, and we have experimented with various combinations. The preparation itself, containing iron, copper, and liver and marrow extracts, is put up in both fluid and capsule form; we have found it very suitable for routine use in the clinic.

Josephs' prescription of iron and ammonium citrate with 0.5 per cent copper sulphate is usually all the treatment needed in a pure nutritional anemia, and even in a severe case it is exceptional that one is unable to bring the hemoglobin to normal in four or five weeks by this treatment. We lay stress on the time element because we do not think it a good thing for a young child to remain anemic any longer than necessary during this period of rapid growth. I have never quite understood the interest of some of my friends in methods of treatment which take months to manifest their effects. It is for this same reason that in any severe case, unless it be of a simple type which is sure to respond rapidly, I like to begin treatment by transfusion.

DR. FRANK NEFF (KANSAS CITY, MO.).—It has come to the stage where we don't know what to do with the detail men who come in with preparations for the treatment of anemia.

Recently we had a child with polycythemia and hyperchromia from too much transfusion. I wonder whether you have seen anything similar from any of these wonderful preparations.

DR. COOLEY.—There are occasional reports of the production of polycythemia even from the administration of iron. That is difficult to explain theoretically. When we began to try bone marrow, we fed it to some of the laboratory technicians. One girl had a hemoglobin of 17 gm. at the beginning of the administration, and after a few weeks it had risen to 21 gm. That is our sole experience.

As to the effect of certain elements in the diet—it seems to me that we do not have any definite basis for estimating this precisely. It has long been recognized

that occasionally one can get better results in the treatment of a nutritional anemia by changing from a poor diet to a good one than by any drug administration. There has been, as you know, a good deal of study of the vegetables, especially with reference to their iron and copper content, though there is probably more to it than this. Practically nothing is known of the value of the cereals. We receive a good many requests from commercial firms to investigate some of these questions.

DR. HUGH L. DWYER (KANSAS CITY, MO.).—In a paper delivered at the meeting of the Milk Commissions yesterday, allusion was made to the giving of egg yolk as a source of iron, and it was stated that fifteen yolks a day would be needed if they were the sole source of iron. We were advised to fortify milk by the addition of a mixture of iron, manganese, and copper. Cereals were shown to have no effect. The paper was presented by a professor of agricultural chemistry at the University of Wisconsin.

DR. ABT.—Have they patented the manganese?

DR. COOLEY.—I am, as I have intimated, not at all sure of the desirability of the routine addition of iron to milk as a preventive of nutritional anemia. If one is to base one's ideas on Helen Mackay's work, one must remember that she seems to have been dealing with a rather inferior group of children, and that the "normal" hemoglobin curve which she obtained by adding iron to the milk was no better than observers in other parts of the world have observed when no special feeding was given.

If iron, iron and copper, or iron and liver were surely a preventive of the common anemia of prematures and twins I should think it worth using. Dr. Abt is one of those who have helped to prove that this anemia is not readily prevented in this way. I believe that this particular anemia is probably due to underdevelopment of the hemopoietic system, in which one would hardly look for much help from drugs. This is a different thing from the anemia due to iron reserve exhaustion, which comes later in the first year, and also to which premature infants and twins are peculiarly susceptible. I believe that proper feeding of the child should take care of this.

DR. DWYER.—What is egg yolk good for?

DR. COOLEY.—It is an excellent food and contains lipids and some vitamins. There is a real use for vitamins in the treatment of some anemias. While there is no particular type of anemia that can be definitely associated with any avitaminoses, children who are so poorly fed as to develop an avitaminosis are likely to have anemia also; if you take care of the vitamin lack, you will help in the cure of the anemia.

DR. BERNARD BERNBAUM (DETROIT).—Do you agree with Isaacs about the use of vegetables? "Why irritate your patients with spinach when you can give them iron?"

DR. COOLEY.—I don't think that the question of the use of vegetables has yet been satisfactorily explored. I should not give them just because of their iron content. They are, however, a part of the good general diet which everyone thinks should be a part of the general regime in any anemia, especially those of the nutritional type.

DR. PRESTON MCLENDON (WASHINGTON, D. C.).—What hemoglobin level do you advise for iron administration?

DR. COOLEY.—That depends on the cause of the anemia, whether it has developed slowly or rapidly. In some anemic states you may have a pretty low

hemoglobin level and get prompt recovery without any special iron treatment. The crises of hemolytic icterus sometimes offer good examples of this. In nutritional anemia, or any "iron deficiency" anemia, I think I should give iron if the hemoglobin were 10 gm. or less, because I like to see the children recover rapidly.

DR. ABT.—I have always followed Czerny's teaching. In 1912, I think, he showed that in those alimentary anemias caused apparently by the exclusive and excessive feeding of milk the patients did better if milk was practically eliminated from the diet.

DR. COOLEY.—Czerny and Glanzmann believed that milk had a definitely deleterious effect in these anemias, which they tried to ascribe to a hemolytic action of the fatty acids. Their work was not, to my mind, very convincing. The idea had a considerable following for some years but has largely been abandoned. You may have read Baar's monograph on the subject. He did just the opposite to the teaching of the Czerny school; he treated the "milk anemias" by giving more milk instead of less and claimed as good results, or better. There is, of course, this much to it—if a child gets too much milk, it will interfere with his taking the good general diet that we think he ought to have. I have never believed that "milk anemia" was an indication for the elimination of milk.

DR. ABT.—Not for elimination, but for cutting down.

DR. COOLEY.—We cut it down to encourage the taking of other things. One of the best things you can give in these cases is meat, which is probably worth more than the vegetables.

QUESTION.—What therapeutic value has ventriculin?

DR. COOLEY.—We have never used it. It has seemed to me that it was brought out to meet a specific indication in pernicious anemia and perhaps in some other achlorhydric anemias of adults and that there are few if any comparable anemias of childhood in which one would expect it to be useful.

We have seen recently what we believed to be a queer response to ventriculin. A child, whose real trouble was hemolytic icterus, was brought to us after prolonged treatment with ventriculin. He had achylia gastrica, pronounced macrocytosis with high color index, and a very high reticulocyte count. The picture might almost have been that of a pernicious anemia in a remission, except for the fact that pernicious anemia does not occur at that age. We stopped all treatment, and in a comparatively short time the macrocytes, which were the queer thing in the picture, had disappeared and been replaced by microcytes. We thought that ventriculin had probably stimulated the macrocyte response.

DR. GEORGE J. FELDSTEIN (PITTSBURGH, PA.).—I have been told by men from southern regions that they see anemia resulting from excessive exposure to the sun. Have you seen anything of this? I suppose that dysentery or parasitic infestation might be a factor. Have you found parasitic infestation a common cause of anemia?

DR. COOLEY.—We have so few cases of parasitic infestation that my knowledge of the anemia they cause comes chiefly from the literature. I have seen a whole family with serious and prolonged anemia due to hookworm. There seem to be two types of anemia caused by quite a variety of parasites. Some, like the hookworm, actually draw blood, causing an anemia of the type due to chronic bleeding. Another type is generally explained as due to toxins produced by the parasites. A few cases of the pernicious anemia caused by the fishworm have been reported in children, but these cases are rare.

I have no knowledge of anemia caused by the sun's rays, but, remembering the marked effects of sunlight on certain types of blonds, I should consider it not impossible.

QUESTION.—What can we say to the otolaryngologists who are always harping on the blood in relation to the chronic running ear we get at this season?

DR. COOLEY.—I think you might say that, if they will cure the ears, you will cure the anemia. There is no doubt about the vicious circle in the alimentary-infectious anemias. The anemia makes the infection worse by lowering resistance. The infection aggravates the anemia. In the more troublesome ones there often seems to be a constitutional susceptibility. It is a difficult chain to break. This is one of the conditions in which I think there is often indication for repeated transfusion.

DR. PHILLIP S. ASTROWE (KANSAS CITY, MO.)—I think that our ideas as to the life of the red cell after transfusion have changed considerably in the last five or six years. Ashby, some fifteen years ago, studying cells transfused from the so-called universal donor, showed that the life of the cell is about sixty days. More recently Lonstetter and Levine, in describing two new blood groups, showed by agglutinin tests that the transfused cells were still in circulation after fifty to seventy days. Another method of studying this is by volume determinations. After transfusion both plasma volume and cell volume are increased. The increase in plasma volume lasts only about forty-eight hours, while the cell volume remains up for four or five weeks, and the hemoglobin volume is increased for nearly as long a time. From these several methods I think we can conclude that the life of the transfused cell is longer than we have been in the habit of thinking.

DR. COOLEY.—I think it is evident that, since the transfused cells must be of very different ages when they are put into the recipient's circulation, they will degenerate and break up after varying times. In the case of which I spoke, in which there seemed to be no hemolysis of the transfused cells, we found that we had to repeat the transfusion on the average every three weeks or less. This did not of course show that some of the cells might not have a considerably longer life.

DR. ABRAHAM B. SCHWARTZ (MILWAUKEE, WIS.).—Have you seen anything in children comparable to what has been reported in adults concerning the relation of the use of amidopyrine to agranulocytosis?

DR. COOLEY.—I have not. There are very few cases of malignant neutropenia reported as occurring in childhood, and some of these have been doubtful. After all, there are not many children to whom one would give this drug, and the proportion of adult users of it who develop the neutropenia is small.

DR. WALLACE B. TAGGART (DAYTON, OHIO).—Do you feel that some children respond to infections with a lymphocytosis where you would expect a leucocytosis?

DR. COOLEY.—A lymphocytic response to pyogenic infection?

DR. TAGGART.—Pneumonic infection.

DR. COOLEY.—I should say that must be a rare experience. In some very severe infections you may see a relative lymphocytosis, but that is due to pronounced marrow hypoplasia or aplasia. Cell responses do vary, of course. Occasionally one sees a pronounced eosinophile increase instead of the ordinary neutrophile response, so that the eosinophiles seem to replace the neutrophiles, but a replacement of granular cells by lymphocytes would hardly be expected.

DR. TAGGART.—I asked the question because in the case I have in mind there was in the early stage some doubt as to differentiation between an infectious proc-

ess and leucemia. After the first count of 17,000 with 85 or 90 per cent lymphocytes, the patient developed bronchopneumonia and the total count doubled, but the differential remained the same.

DR. COOLEY.—I can remember no experience like that.

DR. GERARD N. KROST (CHICAGO).—Have you met with cases of leucemia which went through an aleucemic stage without any evidence of leucemia? I had a patient with a count of about 1,200, with 70 per cent lymphocytes and a high-grade anemia; she lived about eight weeks. For the first six weeks of that time we gave her transfusions, there was rapid blood destruction, but all the lymphocytes were of the mature type. About a week before her death the count went up to 15,000, and practically all the lymphocytes were immature. The platelets, usually reduced in leucemia, were normal until a week or so preceding death, when they dropped rapidly; the spleen became enlarged for the first time; there was slight general adenopathy; and she died with purpuric manifestations. Unfortunately no postmortem was permitted. The final picture apparently was one of leucemia, though for about seven weeks of her illness it had been more like that of infectious anemia with agranulocytosis.

DR. COOLEY.—I think that is one of the most difficult diagnostic problems we have to meet, the question whether a condition like that, when first seen, is a leucemia or an aplastic anemia. I do not think that one can often make a positive diagnosis in the early stages. Most of them prove to be leucemias. We have recently been observing a case in which we changed our diagnosis between leucemia and aplastic anemia about once a week. It proved to be an aplastic anemia. The platelets are usually reduced in leucemia, but I have seen one or two in which they were not down to what I should consider the bleeding level, though there were purpuric symptoms.

DR. HARRY M. GREENWALD (BROOKLYN, N. Y.).—You can often get a better idea of the condition by study of the marrow.

DR. COOLEY.—The leucemic infiltrations are not universally distributed throughout the bones, and in the early stages there may be parts of the marrow that are active for a considerable time. There may be in the course of a leucemia an occasional period of regeneration in which the blood comes back nearly to normal. It seems to me that such a condition is the probable explanation of periods in which the platelets are well up.

DR. GREENWALD.—Some time ago I had occasion to study the marrow in a case of aplastic anemia. From this study and from observations on agranulocytosis I am convinced that in these conditions there must be a constitutional inferiority of the marrow. You are probably familiar with the reports of malignant neutropenia following the use of phenobarbital. I don't think that will occur in a normal individual who has no predisposing peculiarity of the marrow. I gave fairly large doses of pyramidon to a group of children every three days and made careful blood studies. In not a single case were we able to find changes in the total count or types of white cells. We might go on with studies for a long time until we struck a child with a constitutional susceptibility to the drug.

You mentioned the effect of bone marrow. We have been interested to see that in aplastic anemia even though the patient eventually dies the disease seems to be arrested for a time by marrow administration.

DR. COOLEY.—We have seen a temporary effect such as you speak of. The fact seems to be, as I think you pointed out in one of your articles, that in a real aplasia the marrow is not capable of a permanent reaction. In the cases that result from poisoning by x-ray, benzol, etc., I think that there is a possibility of recovery if the destruction has not gone too far because we have a cause which can be

completely removed. In the primary idiopathic form and in most of the secondary states I think we cannot look for recovery.

The matter of constitutional inferiority—diathesis, if you like that word—is one of the most important questions we meet in the whole subject of the anemias. When this is not a factor, it is not difficult to treat most of the anemias. In malignant neutropenia I think that the evidence for a predisposition is very striking. Some of the men are trying to explain it on the basis of an allergic hypersensitiveness to these particular drugs. This is at least plausible.

DR. THURMAN B. GIVAN (BROOKLYN).—Within the last three months we have had in our hospital an Italian boy, with no apparent trace of negro blood, with sickle-cell anemia. His mother also had sickle cells. We removed his spleen, and about six weeks later he died of pneumonia. I thought it might be of interest to add this to those cases already reported.

DR. COOLEY.—They are always of interest. I counted recently fourteen cases, of which I had knowledge, of sickle-cell anemia in white children. Most, but not all, have been in Italian or Greek children. Cooke, of St. Louis, recently had two in what might be called an ordinary American family, with no Mediterranean ancestry. I have no doubt that there are many more of these cases in white children. They are missed because the examination of the moist blood film has so largely gone out of fashion. If this were a part of our ordinary routine, we should be saved some embarrassing experiences, like a recent one in our own hospital, when an Italian boy in an abdominal crisis of sickle-cell anemia was operated upon for appendicitis.

PROF. ARVID WALLGREN (GÖTEBORG, SWEDEN).—Can you tell me whether sickle-cell anemia occurs in Italy and Greece?

DR. COOLEY.—We have seen two patients from the Peloponnesus, but so far as I know none have been reported by Greek physicians. The father of our patients told us that in the region from which they came the people went to herb doctors, almost never to real physicians. I suspect that the same condition obtains in Sicily and Calabria, from which districts our Italian patients seem to come. I know of only one report from Italy, and the illustration of the cells in that was not very convincing.

DR. ROBERT A. STRONG (NEW ORLEANS, LA.).—Are we justified in considering that erythroblastic anemia is confined to the Mediterranean races? Of the reported cases, one was in an English child and another in a negro.

DR. COOLEY.—Those were our cases, and we found on further study that our diagnosis had been wrong. The mulatto (not negro) proved to have hemolytic icterus, and the English child was finally decided to have a secondary hemolytic icterus due to syphilis. All the others have been of Greek, Italian, and, I think, some of Spanish blood. Some reports from South America sound to me like erythroblastic anemia. I am not, however, a great believer in any strict racial limitation of disease. It seems to me to be rather a matter of geographic conditions. Erythroblastic anemia, sickle-cell anemia, and hemolytic icterus are all characterized by prevalence in certain districts and among certain peoples. Hemolytic icterus is now spread pretty well all over the world, but it is found more often in people of German descent and is more prevalent in certain districts of Germany than anywhere else. Possibly it got its start in some segregrated part of Germany. Some similar situation may account for the apparent limitation of sickle-cell anemia and erythroblastic anemia. It is interesting, however, to note that the literature seems to indicate a greater prevalence of splenohepatic diseases of all kinds in the Mediterranean races.

DR. STRONG.—I have noticed that there have been some rather indefinite reports of bone changes in hemolytic icterus similar to those seen in erythroblastic anemia. Are they of the same type?

DR. COOLEY.—We have seen these same rather vague reports of thick skulls and "tower skulls" and have been on the lookout for something of the kind, but we have failed to find it. Gänsslen mentions something of the kind, but he describes also various physical peculiarities and malformations which I do not believe to belong to hemolytic icterus per se; I have suspected (with no definite reason) that his large series came from an isolated community in which there was a good deal of intermarriage with probability of other reasons for developmental abnormalities. Hemolytic icterus is, however, characterized by marrow hyperplasia, which might at times reach the point of causing the radiographic appearances, just as they do occasionally appear in sickle-cell anemia.

DR. STRONG.—What has been the average length of life after splenectomy in erythroblastic anemia?

DR. COOLEY.—I cannot answer that question definitely. Only three patients are now living out of our series from whom the spleens have been removed. One, about ten years old, will probably die within the year. We are keeping her alive by a transfusion every two or three months. The second, about eight years old, is getting along very comfortably and may live for some years. Her younger sister, now about three years old, is subject to severe respiratory infections, in which she goes downhill fast and comes back slowly. One of them may carry her off at any time. In general, the duration of life in these patients seems to depend on the kind of infections they run into. They do not usually die of the anemia, but their resistance is poor. Most of them do not live past the tenth year, though one, originally reported by Stillman in 1927 as von Jaksch's disease, who had an early splenectomy, is still living at the age of twenty-seven years. This is the only arrested case of which I know.

DR. STRONG.—I asked because we have a case under observation at the present time, reported from my department by Williamson a short time ago. The spleen was removed at twelve months. The child is now nine years old. The skin shows a copper bronze Mongolian color, without discoloration of the sclerae, and I cannot see that this has changed at all. The bone changes, however, seem to me even more exaggerated than when the article was published nine months ago. We have been wondering how long we might expect to keep her alive.

DR. GREENWALD.—Do you feel that the Mongoloid appearance of the patients is characteristic of this disease? Don't you find it in aplastic anemia?

DR. COOLEY.—I should not expect it in aplastic anemia because I think that it is due to marrow hyperplasia. When the malar eminences are involved, there is the effect of high cheek bones. So far as the color is concerned, that may be seen in many anemias, but it is only in the conditions with pronounced marrow hyperplasia that we see the thick skull and the high cheek bones.

I think we have laid too much emphasis on this feature because it is so interesting when it is present. It may occur in sickle-cell anemia, which is another disease with marrow hyperplasia. The negro traditionally has a hard skull and rather tough bones in general. It is true that in sickle-cell anemia we do not see the general widening of bone and increase in marrow cavity present in the white child with erythroblastic anemia, but the skull changes do occur in moderate degree.

DR. CHARLES W. MARTIN (Far Rockaway, N. Y.).—I should like to know what rôle you think splenectomy plays in the treatment of some of the grave anemias.

DR. COOLEY.—I touched on that in my preliminary discussion. In hemolytic icterus, hemorrhagic purpura and, we think, erythroblastosis of the newborn, the spleen is apparently directly concerned in the destruction of blood cells, though we do not clearly understand the mechanism of the process. Since this, unlike other splenic functions, is not taken over by other depots of histiocytic tissue after splenectomy, in these conditions the operation usually effects a cure. Since in sickle-cell anemia, erythroblastic anemia, and the secondary hemolytic anemias, the cell destruction seems not to be directly due to splenic activity, the operation has little effect on the disease process. It is worth while to remove the organ sometimes in erythroblastic anemia and in some of the other diseases in which it becomes very large, simply to free the child of the burden of its weight. In "splenic anemia," often looked on as the first stage of Banti's syndrome, splenectomy is frequently advised as a possible preventive of the later development of bleeding and cirrhosis. In the related condition in which splenomegaly and gastric hemorrhage are early symptoms, splenectomy has proved very effective. Both of these disorders seem to depend on vascular changes originating in the spleen, and the operation is supposed to check their further development. It does not always have this effect, however. I mentioned earlier some theoretic possibilities in other disorders.

DR. HENRY F. HELMHOLZ (ROCHESTER, MINN.).—Is the first stage of Banti's disease any easier to recognize than the later stages? How often do you make a diagnosis of Banti's disease?

DR. COOLEY.—That is certainly a rare diagnosis in childhood. Splenic anemia is the wastebasket diagnosis in the anemias of childhood. As nearly as I can state the situation, if you have a condition with splenomegaly, anemia, and leucopenia which persists, and you can rule out all the other things which might cause it (of which I can think of quite a number), you may conclude that this is perhaps the type of splenic anemia which later will develop into the Banti syndrome. If you remove the spleen, you will probably do no harm, and you may prevent the later symptoms. Our only cases of the Banti syndrome have followed splenectomy.

Splenectomy sometimes fails in cases where one would have expected success. One possible reason is the development of accessory spleens overlooked at the time of operation. Another is that while usually other parts of the reticuloendothelium do not take over the pernicious activity of the spleen, occasionally they seem to do this, and after a time the symptoms recur.

DR. GREENWALD.—I think one must warn the patient that splenectomy is not always a permanent cure for hemolytic icterus. In Berlin, I saw a patient who had had a splenectomy for hemolytic icterus and who was presented showing marked improvement. In 1928 I saw the same patient again with a marked recurrence, and practically the same as in 1921 before the splenectomy.

As to Banti's disease—I had occasion to observe a child who had a large spleen and severe hemorrhage. After the hemorrhage the spleen diminished and subsequently increased. Splenectomy was performed, and so far the child has done well. Warthin and others believe that splenic thrombosis is the first stage of Banti's disease. The idea is that, if you operate before the portal vein is involved, you may be able to effect a cure. Wallgren reported a series of patients with thrombosis of the splenic vein whom he had followed for a number of years and who remained well. On the other hand, he says that these children sit on a volcano.

DR. COOLEY.—We have not, in our few operations for this type of disorder, been able to demonstrate thrombosis in the splenic vessels at the time of operation or in the excised spleen, nor has this been a uniform finding in reported cases. It

would simplify matters if we could be satisfied to put this whole rather vague group under the heading of thrombosis of the splenic vein.

DR. JOHN F. SINCLAIR (PHILADELPHIA).—What has been your experience with the use of destructive x-rays on the spleen instead of splenectomy? We had a child of two months with thrombocytopenic purpura, and, being unwilling because of its age to subject it to splenectomy, we spent several months with transfusion, and ultraviolet rays. Finally, knowing that Pancoast had treated several older children with the deep x-ray, we persuaded him to undertake the treatment of this child. After eight treatments his symptoms disappeared, and during the six years' observation since then, his platelets have remained up and he has had no recurrence. He has never, however, recovered the retractile clot.

DR. COOLEY.—There are two possible substitutes for splenectomy. One is the deep x-ray, and the other, ligation of the splenic artery, both of which have been successfully used. I have had little experience with the x-ray treatment. The objection to it is that it is slow. In a case such as yours, in which there is an objection to splenectomy, or in a mild chronic case I think there may be a good indication for its use; in the ordinary case it has seemed to me that splenectomy was preferable. Ligation of the artery might be a useful procedure in case troublesome conditions were met with at the time of operation which would prolong the operation and increase the risk of shock, but under ordinary conditions, once the abdomen has been opened, it would seem to me to be better to take the spleen out.

DR. GREENWALD.—Thrombocytopenic purpura means splenectomy, undoubtedly, in most cases, but there are cases in which it does not stop the bleeding and others in which it is contraindicated. In such cases I should recommend snake venom. I shall report shortly a group of patients benefited definitely by intracutaneous injection of diluted venom. The platelet counts were increased, and retraction of the clot returned. Bleeding ceased in all but one case, in which there was recurrence after several months.

DR. COOLEY.—Would you think it advisable to try the venom always before resorting to splenectomy? I hesitate to recommend splenectomy when I first see a patient with purpura as, on the one hand, so many of them recover without operation and, on the other hand, the operation is not always successful, though we have had no failures. I suppose that it would be wise always to ascertain by marrow puncture the state of the megakaryocytes before going ahead with splenectomy.

DR. GREENWALD.—A trial of the snake venom is harmless. If it fails, you can still resort to splenectomy. I recommended in an article in THE JOURNAL OF PEDIATRICS that marrow puncture should be performed in every case of thrombocytopenic purpura to see if there are megakaryocytes present. If they are, splenectomy is likely to be of benefit.

DR. STRONG.—What type of venom is used?

DR. GREENWALD.—Moccasin venom, diluted 1:3,000. It decreases the vascular permeability, which is the chief reason for the bleeding in purpura.

DR. STRONG.—Moccasin venom is hemotoxic. Might it not cause hemolysis?

DR. GREENWALD.—It does not. Possibly it would if given undiluted, but in this dilution the doses are very minute.

DR. ASTROWE.—How soon does the bleeding stop?

DR. GREENWALD.—In one case of severe hematuria, the bleeding stopped after five days. In a child with a severe epistaxis and extensive subcutaneous effusions, bleeding stopped after forty-eight hours.

DR. ASTROWE.—Does the platelet count come back?

DR. GREENWALD.—It improved in every case, not to the normal count, but to 150,000 or 200,000. In one case it went to normal and dropped back.

DR. ASTROWE.—Do you find bleeding closely related to the platelet count?

DR. GREENWALD.—I have seen a count of 30,000 with no bleeding, and bleeding with a count of 100,000.

DR. COOLEY.—You may have a patient in whose blood you can find only an occasional platelet and who still does not bleed. I have seen only one who bled with as many as 100,000 platelets. Nobody understands the mechanism of the capillary permeability, but there is no question as to its importance in determining the purpuric bleeding.

QUESTION.—Is the effect of the venom more lasting than that of the antivenom?

DR. GREENWALD.—I cannot say. I have read the article to which you refer, reporting the cure of a soldier by the use of antivenom after failure of all other measures to stop extensive bleeding. We tried the antivenom in a severe case of purpura after that report, but it was not successful; we cured the patient by repeated transfusion.

DR. COOLEY.—It is difficult to estimate the value of any method of treatment of purpura because there is so often spontaneous cessation of bleeding and single cases do not prove much.

DR. ELEANOR LESLIE (CHICAGO).—The inconsistency between platelet counts and coagulation time is often due to the fact that the platelets have been broken down by admixture with tissue fluid or contact with glass. In such cases one may find a low platelet count and a short coagulation time. The rapidity with which tissue fluid breaks down platelets often leads to an inaccurate estimation of platelets when the blood is obtained through a puncture wound.

DR. COOLEY.—Mills, of Cincinnati, who has written a good deal about the clotting function, thinks that you get a better picture of what goes on in case of bleeding if you take blood for examination from a finger prick; in other words, if you have tissue fluid mixed with it. I think most of us believe that venous blood is better. One must be careful, in making the venipuncture, not to draw any tissue juice into the needle.

DR. LESLIE.—In order to avoid the breaking down of platelets by tissue fluid or contact with glass, I have been taking blood for platelet counts by venipuncture, receiving the blood into an iced, oiled syringe, and introducing it immediately into paraffined tubes imbedded in ice. The platelet count is made from the plasma after the cells have settled out, and the coagulation time of the plasma is determined in paraffined tubes. If there has been difficulty in obtaining the blood, or if there has been an admixture of cerebrospinal fluid as may happen when the blood is taken from the superior longitudinal sinus, we find low platelet counts and short coagulation times. If there is no admixture of tissue fluid or cerebrospinal fluid, the platelet count is high—in newborns 500,000 to 700,000—and the coagulation time at 25° C. in paraffined tubes, 10 to 20 minutes. Further centrifuging of this plasma in paraffined tubes in ice, yields an upper layer of platelet-free plasma which may have a coagulation time of several hours.

DR. COOLEY.—I have an impression that the whole question of the hemorrhagic disorders and their relation to the clotting mechanism will bear a good deal more study.

ROUTINE MEASURES FOR THE PROPHYLAXIS OF COMMUNICABLE DISEASES

Report of Special Committee on Prophylactic Procedures Against Communicable Diseases

A YEAR ago a committee was appointed from the Academy of Pediatrics to recommend approved procedures for the prophylaxis of the communicable diseases of childhood. The following report duplicates a certain amount of previous effort, but an attempt has been made briefly and explicitly to present directions for the performance of those immunization procedures which are of practical value and necessity. It is unavoidable that a certain amount of personal opinion should enter in selection of procedures and direction for their performance, but in controversial matters we have attempted to follow generally accepted practice in this country without entering into argumentative discussion. The report is offered simply as an outline for the guidance of pediatricians and general practitioners with the hope that it may prove useful. It is not unlikely that certain modifications may be necessary to suit varying conditions and modifications will of course be necessitated by advances in knowledge. Dr. J. E. Gordon, Detroit; Dr. John A. Toomey, Cleveland; Dr. E. B. Shaw, chairman, San Francisco, compose the committee.

DIPHTHERIA

Age.—Immunization should be routine at one year. It is a desirable practice for the physician to send an appropriate notice at the child's first birthday. Prophylaxis may be performed to advantage between the sixth and eighteenth month and should be advocated up to ten years. Nonimmune adults should be protected if they are unusually exposed to infection, as in the cases of medical students, dentists, nurses, social workers, school-teachers, public health workers, and others with occupational hazards.

Material.—Toxoid should be employed for young children. They seldom manifest other than local reactions. Since adults and children more than ten years of age frequently have unpleasantly severe reactions, it is advisable in this age group to employ toxoid in doses initially smaller than those used for younger children. It is permissible to substitute toxin antitoxin in the older age group. Toxoid should never be injected unless the solution is perfectly clear.

Dosage.—Toxoid for infants and children under ten years: Two injections are given at least two weeks apart. It is permissible to lengthen this interval slightly. The first dose is 0.5 c.c., the second, 1.0 c.c. Injections are made subcutaneously in the arm.

The dose of toxoid for persons over ten years: The immunization procedure should be *individualized,* depending upon the reaction produced by an initial small dose of toxoid. The first dose should be 0.2 c.c. In most instances this amount produces no marked reaction and can be followed at intervals of two weeks by a second dose, 0.5 c.c., and thereafter in two weeks by a third, 1.0 c.c. In the event of a reaction after the first small dose the amounts subsequently injected should be cautiously increased, or the same dose repeated. Immunity may be produced by three injections as small as 0.2 c.c. each.

Toxoid is the preferred immunizing agent for persons of all ages, but toxin antitoxin mixture, which produces generally less severe reaction in older individuals, may be used in the older age group although it does not produce immunity with as much

certainty as toxoid. Three successive injections of toxin-antitoxin mixture in amounts of 1 c.c. each should be given from one to two weeks apart.

New immunizing agents are being introduced, which may be desirable to employ when their usefulness has been fully demonstrated. Alum precipitated toxoid is prominent among these. It has the advantage of requiring only a single dose because of the slow rate of absorption. This preparation is used in amounts of 0.5 c.c. to 1.0 c.c. (varying with different preparations) and should be administered by deep subcutaneous injection into the arm.

Indications for Schick Test.—(1) A Schick test preliminary to immunization is unnecessary for children aged less than seven years. For older persons it is desirable to determine the need for immunization by this means. (2) Those who have received diphtheria prevention should be tested six months later for their Schick reactions. This determines the presence or absence of immunity. If the reaction is positive, injections of the immunizing mixture should be repeated. Often a single additional dose will be sufficient.

Schick Test Material.—Diphtheria toxin for Schick tests is supplied in two forms: (1) Undiluted toxin is contained in a small vial, together with a second vial of normal salt solution for diluting the toxin. Dilutions are to be made immediately before the material is used. Diluted toxin is not to be relied upon after one day. (2) Schick test toxin in peptone diluted ready for use can be obtained commercially and is stable for a period of months. This material is particularly useful when only one or two children are to be tested. Experience indicates that it is as reliable as freshly diluted material, and its use is recommended.

Technic of Schick Test.—To perform a Schick test inject intracutaneously 0.1 c.c. of the diluted toxin (representing 1/50 m.l.d. of toxin) into the flexor surface of the forearm at the junction of the upper and middle thirds. A superficial bleb should result.

Reading the Schick Test.—The result of the Schick test should be determined at the end of seventy-two hours. There are then two possibilities—no reaction or a positive reaction. A positive reaction consists of redness, possibly with induration, 1 cm. in diameter or larger; this signifies lack of immunity. If the test is negative, it should be read again on the seventh day. Desquamation and pigmentation often follow the positive reaction.

Schick Test Control.—A control test may be performed on the opposite arm if desired. Similarly diluted toxin, heated to 80° C. for ten minutes, is used for this purpose. Practically a control test is unnecessary, especially in younger age groups where pseudoreactions seldom occur.

Prophylactic Use of Diphtheria Antitoxin.—This is seldom advisable. When the contacts are not to be seen subsequently or are not under close observation, 1,000 units of diphtheria antitoxin may be injected intramuscularly into the lateral muscles of the thigh, halfway between the hip and the knee. By preference the contacts should be separated from the patient, their susceptibility determined by Schick tests and cultures made of the nose and throat for diphtheria bacilli.

Precautions.—When horse serum is to be administered, especially for prophylaxis of disease, the patient should be investigated carefully for evidence of hypersensitiveness to horse serum. Previous injections of horse serum, including toxin-antitoxin mixtures, are significant. Known sensitiveness to horse emanations—horse asthma—is important. The patient may be tested for serum hypersensitiveness by the injection intracutaneously of 0.1 c.c. of a 1:10 or 1:100 dilution of the antitoxin. The appearance within five to thirty minutes of a wheal or a marked zone of erythema about the site of injection is an indication for care in the administration of the full dose. With evident serum hypersensitiveness, a prophylactic dose of anti-

toxin should be given in divided amounts beginning with 1 c.c. of a 1:100 dilution in saline solution. At intervals of thirty to forty minutes increasing amounts of serum may be given until the full dose is completed. Horse serum is best given into an extremity, in such a location that rapid absorption can be impeded, if an immediate reaction ensues, through application of a tourniquet proximal to the site of injection. Epinephrine solution of 1:1,000 should be kept in readiness for combating reactions.

SCARLET FEVER

Active Immunization.—Active immunization through injection of increasing doses of scarlet fever streptococcus toxin weekly for five weeks has been proposed as a preventive measure. It is of value in nursing groups, for the personnel of communicable disease hospitals, in orphanages, and for others intimately and constantly exposed to scarlet fever. It is not recommended as a general public health procedure, since reactions both local and general are frequent, are often severe in adults, and are not altogether absent in children, and for the reason that the degree and duration of immunity have not been definitely established. A number of physicians, however, use it in their private practice.

Tests for Susceptibility.—A test for scarlet fever susceptibility is made by injecting intracutaneously 0.1 c.c. of scarlet fever toxin (supplied by commercial houses for this purpose). This is called the Dick test. Although it is fairly accurate, it must be pointed out that it is not perfectly reliable; persons with negative Dick tests have been known to contract scarlet fever. Tests should be read in twenty-four hours; a positive reaction (lack of immunity) consists of an area of redness or induration at least 1 cm. in diameter.

Convalescent Scarlet Fever Serum.—Convalescent scarlet fever serum in 10 c.c. amounts has been advocated as of value in passive protection. The evidence is inadequate for a definite opinion.

Scarlet Fever Antitoxin.—Scarlet fever antitoxin has been recommended for passive protection against scarlet fever. Its use is frequently accompanied by unpleasant horse serum reactions, and the evidence regarding its value is inadequate for a definite opinion.

TYPHOID FEVER

Typhoid immunization is not to be recommended for universal application. Its use should be restricted to those whose duties bring them in active contact with the infection, such as doctors and nurses; those who travel in regions where the incidence of typhoid is great; and more particularly those whose vacations are spent in regions where the water supply is questionable or the risk of acquiring typhoid is appreciable. In southern rural communities general programs of immunization against typhoid fever have been used to good advantage.

Vaccine.—The usual vaccine is designed to protect against typhoid, paratyphoid A, and paratyphoid B. Injections should be given at intervals of one week. The first dose is 0.5 c.c., the second and third dose, 1 c.c. each. Injections may be given from five to fourteen days apart, but a reaction from the previous injection should have disappeared before administering the next.

Duration of Immunity.—Immunity after typhoid immunization lasts at least two years. Typhoid immunity cannot be determined by any laboratory test. If protection is to be assured beyond that time, a second course of injections should be given. Where continued protection is essential, one dose may be given each year following the original course of three.

WHOOPING COUGH

Vaccine.—If any good is to be derived from the use of vaccines, they should be prepared from freshly isolated strains and should be given in sufficiently large doses to provoke fever.

Indications.—Prophylactic immunization is commonly employed in the case of those who have been exposed to the disease. Its beneficial effects are uncertain. Vaccines ordinarily contain five to ten billion killed organisms per centimeter. Successive doses of 0.25, 0.5, 1.0, and 1.5 c.c. are given at intervals of two to three days. The same vaccine is used with uncertain success after the development of the disease.

Sauer has recently recommended routine immunization of children against whooping cough, comparable to the program for diphtheria prevention, and advocates large doses of freshly prepared vaccine prepared from organisms grown on human blood medium.

Convalescent Serum.—Convalescent serum from patients recovered from whooping cough has been used by a few physicians in amounts of 10 c.c. for children known to have been exposed to the disease. The evidence in favor of this procedure is indefinite.

MEASLES

There is no method for active protection against measles. The disease may be prevented, or better, modified by the injection of the blood serum of a person recently convalescent from the disease or by the injection of the blood or blood serum of most adults.

Convalescent Serum.—Human blood serum taken one to three weeks after the fever of measles has subsided contains protective substances against the disease. When administered shortly after exposure in doses of 10 c.c. intramuscularly, it may protect against the disease. It usually lessens its severity and is particularly recommended when exposure occurs during the course of another illness, especially respiratory infections. Under ordinary circumstances it is more desirable to produce modified measles than to protect completely. Ten cubic centimeters of serum given on the sixth day after exposure to a person in continuous contact (i.e., on the second day that the patient has the rash) produces partial protection. The contact usually develops measles in a mild form with little or no fever and an atypical rash. Convalescent serum given in ordinary amounts more than seven days after exposure is without much effect.

Adult Blood.—About 30 c.c. of normal whole blood or 20 c.c. of normal serum is said to produce an effect equivalent to that of 10 c.c. of convalescent serum. Measles modified by convalescent serum or normal blood apparently produces a permanent immunity comparable to that from an ordinary infection.

SMALLPOX

Vaccination.—During epidemics of smallpox, vaccination may be performed at any age. All children should be vaccinated between the sixth and twelfth month of age. This should be repeated whenever the disease is epidemic or in the presence of unusual likelihood of exposure, as in foreign travel.

Material.—Any glycerinated vaccine may be used. A record should be kept of the lot number of the vaccine.

Location.—Vaccination may be done on any skin surface; usually the arm or the leg is used. The preferred site is the inner aspect of the arm, at the junction of the lower and middle thirds.

Preparation.—The site should be thoroughly washed with soap and water, scrubbed with 95 per cent alcohol and allowed to dry.

Multiple Pressure Method.—A drop of the virus is placed in the center of the cleansed area. Holding a small sterile needle parallel to the skin surface, the needle is quickly stroked against the skin through the drop of virus; about ten to cfteen strokes are sufficient. The excess of virus may be removed with sterile gauze.

Dressings.—Tight constricting dressings or shields are to be *strictly* avoided. Two or three thicknesses of sterile gauze may be placed over the area and lightly fixed with adhesive tape, in such a way that constriction of the area is avoided. It is permissible to apply no dressing.

Kinds of Reaction.—(a) In a successful primary vaccination, a pustule is present at the end of seven days, usually appearing about the fifth day. (b) An unsuccessful vaccination shows no reaction to the virus and confers no protection against smallpox. Those who fail to react after a primary vaccination with the production of a pustule should be promptly revaccinated. (c) Persons revaccinated after a previously successful result may show a reddened, inflamed macular or maculopapular area at the vaccination site at about forty-eight hours, an immunity reaction. This is evidence of persistent immunity from the previous vaccination.

Successful vaccination wounds may be left alone except for protection against secondary infection. The application of mildly antiseptic solutions of gentian violet, mercurochrome, or merthiolate is useful for this purpose. A secondary infection of the pustule may be cleansed with ether and painted with a mild antiseptic dye. Healing is usually complete after two weeks.

Smallpox vaccination and diphtheria immunization should be done at about the same period of infancy and may be combined. It is convenient to vaccinate at the same visit at which the second dose of toxoid is given.

POLIOMYELITIS

The risk of acquiring the disease is statistically small. Convalescent serum and normal serum have been proposed for passive protection during epidemics. The value of this procedure has not been conclusively demonstrated.

EPIDEMIC MENINGITIS

No present method for active or passive protection.

MUMPS AND CHICKENPOX

Blood serum from recent convalescent individuals has been used for protection against these diseases. Their value is not unquestionably proved and is practically limited to institutions. Indications for such use are not frequent because of the mildness of these infections.

RABIES

Rabies prophylaxis is necessitated by the bite of a rabid animal and is advisable whenever there is a possibility that secretions of a rabid animal have been brought in contact with the abraded skin or mucous membrane. It is important that treatment be instituted at the earliest possible moment. Contaminated abrasions or bites should invariably be cauterized with fuming nitric acid. Other antiseptics have been less satisfactory. Prophylactic treatment should be most energetic following wounds in close proximity to the central nervous system, in those of an extensive nature, and in which treatment is delayed; less heroic measures are permissible with more distal and superficial lesions.

The original method of Pasteur is not now commonly used. Different preparations are supplied by various commercial houses, but they have the common property of being emulsified rabbit cord infected with *fixed* virus which has been killed (in some cases simply attenuated) by the use of chemicals or physical agents. All preparations share the common property of being incapable of producing rabies in the human being as a result of injection. The Semple preparation, a phenolized cord emulsion, is most commonly recommended. The Cumming and Harris methods are employed by some manufacturers.

The prophylactic treatment usually consists of fourteen daily injections of the dose recommended by the commercial house. Injections are given subcutaneously, usually into alternating sides of the abdominal wall, but may be given elsewhere with equally good effect. In cases in which there is extensive injury or if the injury is in close proximity to the central nervous system or if there is more than usual suspicion of rabies, twenty-one or twenty-eight injections should be employed. Sometimes it is recommended that injections be given twice daily if the nature of the case indicates urgent and intensive immunization.

TETANUS

Tetanus antitoxin should be used prophylactically in cases in which there is danger of contamination of a wound with horse manure or human excreta. It is particularly indicated in puncture wounds and wounds about the head.

The prophylactic dose is 1,500 units injected subcutaneously. This may be repeated at intervals of five days if the danger of infection is particularly great. In using tetanus antitoxin as a prophylactic measure, the same precautions should be observed as are recommended for diphtheria antitoxin.

PEDIATRIC DEPARTMENTS IN GENERAL HOSPITALS

(Continued)

Report of the Committee on Hospitals and Dispensaries, American Academy of Pediatrics

REGIONS III and IV include the midwestern and far western states. In Region III, ten states report that one or more general hospitals have at least twenty-four beds and bassinets for infants and children. These ten states are Colorado, Illinois, Indiana, Kansas, Michigan, Minnesota, Missouri, Nebraska, Ohio, and Wisconsin. In Region IV only California and Washington report pediatric departments in general hospitals of the above minimum number of beds.

Table I presents the distribution of the respective services by regions and by states and also reveals the relative size of the services.

Ten states are represented in Region III and two, in Region IV; there are sixty-five hospitals in the former and fourteen in the latter region, representing a total bed capacity of 2,707 and 878, respectively; bassinets number 1,697 and 505 in the same order. The largest single service is found in California, one hospital there reporting 270 beds for children. Second and third largest services are found in Michigan and Ohio with 200 and 100 bed services respectively. The hospital having the greatest number of bassinets is again found in California, the largest service there having 120 bassinets; Michigan reports the next largest with 102 bassinets and Wisconsin is third with 75.

None of the hospitals in either region reports less than twenty beds for children. In Region III Ohio has twenty hospitals which report pediatric services of the size considered in this report, more than twice as many as found in any other state. California in Region IV reports twelve such services.

Residents.—In Region III, fifteen hospitals employ twenty-six pediatric residents. Only thirteen of these residents give their time exclusively to the pediatric department. In each instance the resident receives a salary. These salaries vary from $20.00 to $150.00 per month. In Region IV, ten hospitals employ fifteen residents among whom seven confine their activities exclusively to the pediatric department. The salaries in this instance vary from $10.00 to $125.00 per month.

Internes.—In Region III, six hospitals are found to have a total of twelve internships in which the internes may devote their time exclusively to pediatrics. Region IV has six such interneships in three different hospitals.

Attending Staff.—In Region III among sixty-five hospitals there are 295 pediatricians on the attending staffs. In Region IV, ninety-six staff members are reported. The period of service varies from one to twelve months. Many services are reported of three or four months, but the majority seem to be for a twelve-month period.

Newborn Service.—In Region III, thirty-one hospitals, or about 50 per cent, maintain the newborn service under the supervision of the pediatric department. In Region IV, eight hospitals, or about the same percentage, maintain such services, all of them being in California.

Nursing.—In Region III a head nurse is in charge of the pediatric department in all hospitals. These nurses have had special pediatric training in all but three instances. Again as has been found frequently in the reports on Regions I and II, these nurses in many instances have had only three or four months of special pediatric

TABLE I

STATE	NUMBER OF HOSPITALS	TOTAL BEDS	TOTAL BASSINETS	LARGEST NUMBER OF BEDS IN ONE HOSPITAL	SMALLEST NUMBER OF BEDS IN ONE HOSPITAL	LARGEST NUMBER OF BASSINETS IN ONE HOSPITAL	SMALLEST NUMBER OF BASSINETS IN ONE HOSPITAL
Region III							
Colorado	3	83	70	38	20	45	5
Illinois	8	247	159	47	25	50	3
Indiana	5	182	133	58	25	57	5
Kansas	3	124	61	52	32	26	15
Michigan	8	517	311	200	29	102	4
Minnesota	5	199	112	70	25	33	5
Missouri	5	203	199	70	25	66	12
Nebraska	3	77	46	28	24	20	6
Ohio	20	843	500	100	24	74	2
Wisconsin	5	232	106	80	33	75	10
Total	65	2707	1697				
Region IV							
California	12	807	404	270	27	120	15
Washington	2	71	101	36	35	51	50
Total	14	878	505				

training. In Region IV all hospitals have a head nurse in charge of the pediatric department. In two instances these nurses have not had special pediatric training. However, it is in contrast to note that there are very few instances in which the head nurses have not had one year or more of special pediatric training.

Fifty-eight hospitals in Region III have student nurses, the average service being from two to four months. These nurses may have from one to twenty-five infants under their care, the average being about four to six in a children's department of from one to sixteen children (average of four to eight). In Region IV, thirteen hospitals have student nurses, and the relative number of nurses to care for the infants and children is about the same as in Region III.

Social Service.—Twenty hospitals in Region III and five in Region IV maintain a special social service department for children.

Diet Kitchen.—In Region III, fifty hospitals have a special diet kitchen for infants and twenty-nine have one for children. In Region IV, ten have one for infants, and six have one for children.

Schooling.—Twenty hospitals provide schooling for patients in Region III, and five provide it in Region IV.

Recreation.—Thirty hospitals provide for recreation in Region III and six, in Region IV.

Dispensary.—In Region III, forty hospitals maintain a dispensary for infants and children. Most of these clinics are open daily, and the attendances average from fifteen to thirty patients per day. The extremes in variation of attendance are as low as one and as high as forty-seven per day. In Region IV, eleven hospitals maintain a dispensary for infants and children with attendance figures similar to those in Region III with extremes of as low as eighteen and as high as 125.

In Region III the same staff serves in both hospital and dispensary in thirty-seven instances. The resident receives experience there in thirteen, and the internes, in thirty-one instances. In Region IV these figures are ten, seven, and nine, respectively.

Table II presents figures concerning admissions, deaths, autopsies, and percentage of deaths and autopsies among the hospitals in Regions III and IV.

COMMENT

As might be expected in relatively denser areas of population, we find in Region III a fairly large number of hospitals with pediatric departments of twenty-four or more beds. However, nearly one-third of the total is found in one state, Ohio, and over 55 per cent among three of the ten states in that region. Specifically they are in Ohio, Michigan, and Illinois.

Hospitals which can be considered in this report are found in only two states of Region IV, California and Washington. Fourteen hospitals are reported from these two states, twelve, or over 85 per cent, of them are in California. However, these two states have available about one-third as many beds and bassinets as reported for the ten states of Region III.

Only fifteen hospitals of the entire group in both regions employ pediatric residents. Although twenty-six residents are reported, only half of this number give their time exclusively to the pediatric departments.

Only eighteen interneships in which a man may spend his time exclusively in pediatrics for one year are reported, and these are available only in nine hospitals.

Little need be said here concerning attending staffs, except that, in common with previous reports on Regions I and II, we find too many instances in which services are only for one, two, three, or four months' duration. We wish again to emphasize, at the risk of boring, that to our mind this is too short a time if that service is to be efficiently conducted.

TABLE II

STATE	NUMBER ADMITTED		DEATHS		AUTOPSIES		PERCENTAGE OF DEATHS		PERCENTAGE OF AUTOPSIES	
	NEWBORN	CHILDREN	NEWBORN	CHILDREN	NEWBORN	CHILDREN	NEWBORN	CHILDREN	NEWBORN	CHILDREN
Region III										
Colorado	1527	4953	106	88*	27*	46*	6.9	1.7	25.4	52.2
Illinois	3111	5154	117	112	46	45	3.7	2.1	39.4	40.1
Indiana	1996	3366	100	183	8†	29*	5.0	5.4	8.0	15.8
Kansas	833	680*	16	47*	8	15*	1.9	6.9	50.0	31.9
Michigan	5356	6190*	192*	350*	93*	139*	3.5	5.6	48.4	39.7
Minnesota	2196	3015	94	141	54	90	4.2	4.6	57.4	63.8
Missouri	4366	4044	141	146	36	89	3.2	3.6	25.5	60.9
Nebraska	1350	1678	51	57	30	31	3.7	3.3	58.8	54.3
Ohio	10416	11784	445	656	210	288	4.2	5.5	47.1	43.8
Wisconsin	3594	4388	164	122	26	61	4.5	2.7	15.8	50.0
Total	34744	45252	1426	1902	538	833	4.1	4.2	37.7	43.7
Region IV										
California	7585	9711	275	687	99	186	3.6	7.07	36.0	27.0
Washington	1770	714	6*	6*	2*	1*	?	?	?	?
Total	9355	10425	As there are only two hospitals reported from Washington the failure of one to report figures as indicated above prevents accurate summary figures.							

*One hospital did not reply.
†Two hospitals did not reply.

Only thirty-nine, or about 50 per cent, of the hospitals in both regions maintain their newborn service under the supervision of the pediatric departments. Without wishing to seem impertinent, we suggest that these figures show considerable room for improvement. California has the best record of any state in the two regions in this respect with a figure of 75 per cent; Nebraska is next with 66⅔ per cent.

Nursing care, as far as we can determine from the rather sparse information afforded by the questionnaire, is in most instances competent, although we again find too many head nurses who apparently have not had what we consider adequate pediatric training.

About 30 per cent of the hospitals in Region III and 40 per cent in Region IV mention a social service department for children. These are fairly good figures when one considers that many of the pediatric departments are small.

A large majority of hospitals in both regions maintain special diet kitchens for infants and many have one especially for children.

Less than 33 per cent in Region III and about 50 per cent in Region IV provide schooling for convalescents, while recreation is provided among about 50 per cent of hospitals in both regions. These latter figures again reveal that these two activities probably do not receive enough emphasis in many hospitals. Of course, in the smaller departments there are probably relatively few patients whose stay in the hospital is to be long.

Newborn mortality rates vary considerably for the various hospitals and states. In some hospitals the mortality rate is extremely low and probably reflects excellent obstetric and pediatric care, while among other institutions it is lamentably high. By state as well, there is quite a variation in these figures as evidenced by Nebraska with the low figure of 1.9 per cent and Colorado with a high one of 6.9 per cent. The total average of all states is 4.1 per cent, which is too high.

Alertness of medical thought and efficiency of medical procedure in hospitals is often reflected rather accurately by necropsy figures. Again we find a wide variation in our figures from a low of 8.0 and 15.8 per cent among infants and children, respectively, in Indiana to a high of 58.8 per cent for Nebraska among children and 63.8 per cent for Minnesota among infants.

This is the third report in an attempt to obtain much needed information concerning pediatric care in general hospitals of this country. In previous reports hospitals in Regions I and II of the American Academy of Pediatrics have been considered. A final report will be made in which the committee will attempt to coordinate the three previous reports and from that information to give concrete suggestions as to what should be done to improve pediatric care in general among the hospitals included in the report.

Academy News

The fifth annual meeting of the American Academy of Pediatrics will be held June 7 and 8, 1935, at the Waldorf-Astoria Hotel, New York City.

The program has been announced as follows:

Friday, June 7, Panel Discussions.

9:30 A.M.—"Indications for Surgery in Pyuria," Chairman, Dr. Hugh Cabot, Rochester, Minn.

11:00 A.M.—"Prevention of Colds in Children," Chairman, Dr. Lee Wallace Dean, St. Louis, Mo.

2:00 P.M.—Round Table Discussions.

Subject	Leader
"Adolescence"	Dr. Borden S. Veeder
"Bacillary Dysentery"	Dr. Wilburt C. Davison
"Blood"	Dr. Thomas B. Cooley
"Chronic Lung Conditions"	Dr. Isaac A. Abt
"Diabetes"	Dr. Henry R. Geyelin
"Eczema"	Dr. Lewis Webb Hill
"Encephalitis"	Dr. Josephine B. Neal
"Heart"	Dr. Hugh McCulloch
"Newborn"	Dr. Arthur H. Parmelee
"Osteomyelitis"	Dr. Arthur Krida
"Poliomyelitis"	Dr. John A. Toomey
"Prematurity"	Dr. Julius Hess
"Tuberculosis"	Dr. Chester A. Stewart
"Whooping Cough"	Dr. William H. Park
"Recent Advances in Nutrition"	Dr. H. C. Sherman

8:00 P.M.—Joint meeting of state chairmen and the committees on child health relations, school health and school health education, and hospitals and dispensaries.

Fellows are invited but are not permitted to join in the discussion except through state chairmen.

Saturday, June 8

9:30 A.M.—General Meeting

President's address

Report of the executive board
Report of secretary-treasurer
Report of regional committees
Report of special committees.

(Reports will be presented in mimeograph form to the membership)

Panel Discussions

2:30 P.M.—"Pituitary Glands," Chairman, Dr. R. G. Hoskins, Boston, Mass.

4:00 P.M.—"Nutrition," Chairman, Prof. E. V. McCollum, Baltimore, Md.

There will be approximately twenty-five commercial and five scientific exhibits. These will be in the registration room and the Jade Room through which one must pass to go to the meeting hall.

An announcement concerning railroad rates will be made later.

All members should make reservations for hotel accommodations. Special registration cards will be given all members. Regardless if they stay at the hotel prior to the convention or immediately following the meeting, the same special schedule of rates will apply.

Dr. Harry C. Berger, Kansas City, Mo., has accepted the state chairmanship for Missouri.

Dr. Sterling H. Ashmun, Dayton, Ohio, has been appointed state chairman for Ohio.

News and Notes

Members of the American Committee for the International Pediatric Congress to be held in Rome, Italy, in 1936, are as follows:

American Pediatric Society: Dr. Henry F. Helmholz, Dr. Clifford G. Grulee, and Dr. L. Emmett Holt, Jr., secretary of the American committee.

American Academy of Pediatrics: Dr. C. Anderson Aldrich, Dr. L. R. DeBuys, and Dr. Clifford G. Grulee.

Section on Pediatrics of the American Medical Association: Dr. Fred W. Schlutz, Dr. Alexis F. Hartmann, and Dr. Frank C. Neff.

Those who have been chosen so far by the committee to appear at the Congress are: Dr. James L. Gamble, "Relatori" on the subject, "Mineral and Water Metabolism in Childhood and Its Relation to the Problem of Artificial Feeding"; Dr. Chester Stewart, "Relatori" on the subject, "The Problem of Childhood Tuberculosis"; and Dr. Bronson Crothers, "Correlatori" on the subject, "Neuropsychiatric Diseases in Pediatrics From the Clinical and Social Point of View."

The Society for Pediatric Research will meet on Tuesday, May 7, 1935, at the Chalfonte-Haddon Hall in Atlantic City. There will be a morning and afternoon program. Dr. A. A. Weech of New York is secretary of the Society.

The American Pediatric Society will hold its annual meeting at the Wade Park Manor in Cleveland, Ohio, on May 2, 3, and 4, 1935. Dr. Hugh McCulloch, of St. Louis, is secretary of the Society.

The Section on Pediatrics of the American Medical Association will meet in Atlantic City at the time of the general meeting, June 12, 13, and 14, 1935. This meeting will be a joint one with the Canadian Medical Association, and it is expected that the meeting of the scientific assembly will be a most unusual one.

The South Carolina Pediatric Society held its annual meeting at the Jefferson Hotel, Columbia, S. C., on Monday, February 11, 1935. Dr. E. C. Mitchell, of Memphis, Tenn., was a guest of the Society and conducted a round table discussion on the subject, "Tonsils." A motion was carried that the attitude of the Society on this question should be made public in the lay press of the state and also to the state medical association. Approximately 80 per cent of the pediatricians of South Carolina were present, as well as many otolaryngologists.

Dr. William Weston, Jr., of Columbia, was elected president; Dr. Thomas Dotterer, of Columbia, vice-president; and Dr. Leland Salters, of Florence, was re-elected secretary-treasurer.

A recent meeting of the Texas Conference on Child Health and Protection was held with Dr. E. G. Schwarz, of Fort Worth, as chairman of the medical section. He was assisted by: Dr. T. J. McElhenney, Austin, Dr. L. O. Godley, Fort Worth, Dr. Mary Harper, San Antonio, Dr. Howard Granberry, Austin, Dr. M. S. Wheeler, Austin, Dr. Edythe P. Hershey, Dallas, and Dr. C. D. Reece, of the State Health Department. The meeting was well attended and the program well received by the lay workers present.

May Day-Child Health Day has become an established institution throughout the United States. It was inaugurated in 1924 by the American Child Health Association for the purpose of calling the attention of parents, communities, and the public in general, to the need for measures to protect the health of children.

In 1928 the United States Congress passed a joint resolution designating May 1 as Child Health Day, and authorizing the president to issue a proclamation requesting national observance of the day.

In 1929 the Conference of State and Provincial Health Authorities of North America appointed a May Day Committee, which in 1932 took over from the American Child Health Association, with the continuing assistance of that organization, the responsibility for the annual observance of Child Health Day. In the states the work is under the direction of state departments of health.

The May Day-Child Health Day project for 1935 is diphtheria immunization. It was chosen because there has been but little reduction since 1930 in the number of deaths from diphtheria throughout the country.

"*Immunize now—stamp out diphtheria*" is the slogan.

The measures proposed are:

To immunize all children between the ages of six months and six years.

To make early immunization a routine practice by physicians in the future.

The goal of the work is *no deaths from diphtheria.*

In order to obtain the cooperation of physicians, it was suggested to each state health officer that he send a communication to each physician in his state urging:

That he remind his patients who have children under school age of the need for immunization;

That he ask his patients to bring their children to be immunized;

That in the future he make it a routine of his practice to immunize, during the first year of life, all babies under his care.

Many state health officers have responded enthusiastically to this suggestion. The majority of pediatricians do immunize early as a matter of routine. It is desired that physicians in general practice do likewise. Plans for this should be worked out by local medical societies in conjunction with the departments of health. Members of the American Academy of Pediatrics have been asked to assist.

This project will tend to place the responsibility for diphtheria immunization on the physicians, where it rightly belongs. Each member of the American Academy of Pediatrics should be counsellor and guide in this work in his own community.

The following men have been certified by the American Board of Pediatrics since the last report:

Louis H. Barenberg, New York, N. Y.
Stanley Brady, New York, N. Y.
F. H. Clark, Jamestown, N. Y.

Harry O. Davidson, Detroit, Mich.
Clair L. Douglas, Detroit, Mich.
Ethel Collins Dunham, New Haven, Conn.
William Littell Funkhouser, Atlanta, Ga.
Linton Gerdine, Athens, Ga.
Jesse Robert Gerstley, Chicago, Ill.
Murray Burnes Gordon, Brooklyn, N. Y.
Benjamin Hoyer, Cincinnati, Ohio
W. Lloyd Kemp, Detroit, Mich.
George Clifford King, Fall River, Mass.
James Hall Mason Knox, Jr., Baltimore, Md.
A. Max Kohn, Detroit, Mich.
John Allison Nunn, San Antonio, Texas
Harry D. Pasachoff, New York, N. Y.
Donald Wallace Porter, New Haven, Conn.
L. J. Schermerhorn, Grand Rapids, Mich.
Philip H. Sylvester, Boston, Mass.

Correspondence

London, W. 1., February 16, 1935.

Comment was made last May on the subject of malnutrition and physical unfitness in children in relation to the economic difficulties existing in certain sections of the population in England at the present time. In this connexion the recently published annual report of Sir George Newman, Chief Medical Officer to the Board of Education, is of interest. During the year covered by the report, 3,000,000 school children passed under medical review, and 2,000,000 re-inspections were carried out. Three hundred and sixteen local educational authorities submitted figures, from which the mass return of 1933 was compiled, and it shows that the condition of school children throughout England and Wales during this period demonstrated no deterioration when compared with the two preceding years. Sir George Newman therefore concludes that, in spite of distressing economic and social difficulties, the general health and nutrition of school children has on the whole been well maintained.

It should be mentioned in this connexion that two committees set up to investigate and report upon the question of diets adequate for the maintenance of good health recently issued their reports, which gave rise to some controversy. The one committee appointed by the Ministry of Health regarded as adequate a dietary containing rather less first-class protein and somewhat lower in total caloric value than that recommended by a similar committee appointed by the British Medical Association. Both committees numbered among their members persons of unquestionable authority on the subject under investigation. As might be expected, political capital was made of the fact that the scale was lower in the report issued by the committee of the Ministry. However, it was obvious to a critical scientific observer that the differences between the two reports were more apparent than real, and the wise course was adopted of arranging a meeting between representatives of both committees. As a result a statement was issued making clear the reason for the differences which existed, and thus showing cause for dispute. One of the points of difference was in regard to the question of increased amounts of milk for children, advocated by the British Medical Association committee, and at the present moment it has been conceded that any school teacher can authorise the provision of free

milk to be given at school to a child considered to be under-nourished, pending the next school medical inspection, when the medical officer in charge will review the case.

As is probably well known, a further effort is being made by the osteopaths to obtain official registration and state recognition in this country. The bill aimed at effecting this has just passed its second reading in the House of Lords. The Lord Chief Justice, in the course of the debate, said that as a mere lawyer he was staggered by the bill which, among other things, would allow an osteopath to sign a death certificate. Lord Moynihan and Lord Dawson (President of the Royal College of Physicians) both opposed the bill, pointing out from a professional point of view the monstrosities of the measure and the adverse influence it would have on the interests of the laity themselves. The medical profession generally is entirely opposed to the registration of osteopaths, who appear by the terms of the bill to be trying to create a method of carrying out medical practice in its fullest sense without having conformed with the minimum requirements of the General Medical Council. After once obtaining a legal medical qualification in the usual manner, a practitioner is allowed to practise in this country any method he may choose, but any attempt to obtain full recognition to practise without ordinary preliminary and clinical training appears to be a back-door method of entering upon medical practise, and a dangerous one.

The Goulstonian Lectures, three in number, are to be given this year in March, before the Royal College of Physicians, by a paediatrician, Dr. Alan Moncrieff, his subject being "Respiratory Failure, Including the So-called Asphyxia Neonatorum."

During this winter the meetings of the Children's Section of the Royal Society of Medicine, under the presidency of Dr. R. Jewesbury, have maintained their past standard of clinical interest, and one new feature has been the devoting of one meeting to the re-showing of cases previously demonstrated and discussed.

The British Paediatric Association is meeting this year on the third and fourth of May, at Newcastle, County Down, in Northern Ireland; Dr. Hugh Thursfield is this year's President, and Dr. A. G. Maitland-Jones is now the Secretary. This will be the first meeting of the Association to have taken place in Ireland.

K. TALLERMAN.

Erratum

On page 40 of the article, "Hemorrhage and Subsequent Calcification of the Suprarenal," by Charles E. Snelling, M.B., and I. H. Erb, M.B., the third sentence in the fifth paragraph of the summary should read, "In *the eight with calcification* there was definite evidence of previous hemorrhage into the gland."

Comments

THE truth of the frequently repeated statement that the high maternal mortality rate of the United States when compared with the rate for foreign countries was due in a large part to differences in recording deaths, and hence was not real, has been rudely shattered by a recent study of the Children's Bureau.* In continuing a study of the Third White House Conference, a sample group of 1,073 deaths occurring in 1927 and certified by attending physicians as puerperal were selected and the pertinent information from 477 of these sent to the vital statistics division of twenty-four foreign countries, with the request that they be classified in accordance with their rules and regulations for classifying deaths. No information as to how they had been classified in the United States reports was given. Replies were received from sixteen countries. The rate for the United States was then checked according to the way the deaths in the United States would have been recorded in each country. In this way a definite basis of comparison between the United States and foreign countries was established.

The rate for the United States remains at the top of the list, 64.7 per 10,000 live births. Scotland has practically the same rate, 64.3. Norway has the lowest rate, 24.5. Next lowest comes Italy, Sweden, and France with 26.4, 27.8, and 28.7, respectively. The rate for England and Wales is 41.1 and for Canada, 55.5. It is thus quite obvious that differences in method of assignment are insufficient to explain the high maternal mortality rate in the United States. Differences in live births as well as differences due to incompleteness of birth registration are negligible factors in the maternal mortality rate. The problem returns to one of medical care and oversight, or, in brief, better obstetrics.

AS A rule it is not the policy of the Journal to publish long papers such as the study of fat metabolism which appears in this issue. The Editorial Board felt that this particular study by Dr. Holt and his associates was so thorough and of such fundamental importance that it ranks as one of the best contributions that has appeared from an American pediatric clinic. Arrangements were therefore made to increase the size of this number of the Journal so that the usual variety and scope of contributions should not be curtailed because of the length of this particular paper.

THE American Child Health Association is sponsoring diphtheria immunization for its 1935 May Day project. Its plans are formulated along the line of urging parents to take their preschool children to a physician for immunization. Members of the Academy are requested to help in working out the local state and community programs.

*Comparability of Maternal Mortality Rates in the United States and Certain Foreign Countries, Elizabeth C. Tandy, D.Sc., Bureau Publication No. 229, Children's Bureau, Dept. Labor, Washington, D. C., 1935.

The Journal of Pediatrics

CONTENTS FOR APRIL, 1935

Original Communications

Studies in Fat Metabolism. I. Fat Absorption in Normal Infants. L. Emmett Holt, Jr., M.D., Herbert C. Tidwell, Ph.D., Claude M. Kirk, M.D., Dorothea M. Cross, and Sarah Neale, Baltimore, Md. ---- 427

Studies in Fat Metabolism. II. Fat Absorption in Premature Infants and Twins. Herbert C. Tidwell, Ph.D., L. Emmett Holt, Jr., M.D., Howard L. Farrow, and Sarah Neale, Baltimore, Md. ---- 481

Studies in Infantile Allergic Eczema. II. Serum Lipids, With Special Reference to Saturation of the Fatty Acids. Harold K. Faber, M.D., and Dorothy B. Roberts, San Francisco, Calif. ---- 490

The Effect of Fever Therapy on Rheumatic Carditis Associated With Chorea. Lucy Porter Sutton, M.D., and Katharine G. Dodge, M.D., New York, N. Y. ---- 494

Virus Encephalitis. Edward L. Bauer, M.D., Philadelphia, Pa. ---- 512

Soy Bean (Vegetable) Milk in Infant Feeding. Fred Rittinger, M.B. (Tor.), Leon H. Dembo, M.D., and Gilberta G. Torrey, Cleveland, Ohio ---- 517

Range and Standard Deviations of Certain Physical Measurements in Healthy Children. William Palmer Lucas, M.D., and Helen Brenton Pryor, M.D., San Francisco, Calif. ---- 533

The Effect of Placental Extract on the Dick Test. Alan Ross, M.D., Montreal, Quebec ---- 546

Pediatric Clinics

The Children's Department of the London Hospital, England. K. H. Tallerman, M.A., M.D., M.R.C.P., London, England ---- 549

Critical Review

Allergic Diseases. Francis Scott Smyth, M.D., San Francisco, Calif. ---- 555

American Academy of Pediatrics

John Ruhräh—In Memoriam ---- 566

Proceedings: Fourth Annual Meeting of the American Academy of Pediatrics. Round Table Discussion on Disorders of the Blood ---- 569

Proceedings: Routine Measures for the Prophylaxis of Communicable Diseases 586

Proceedings: Pediatric Departments in General Hospitals (Continued) ---- 592

Academy News

Academy News ---- 597

News and Notes

News and Notes ---- 598

Correspondence

Correspondence ---- 600

Comments

Comments ---- 602

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